JANUARY, 1952

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

The Role of the Phrenic Nerve in Vagotomy and in Gastrointestinal Mechanisms

The Use of ACTH in the Treatment of Ulcerative Colitis

Single and Multiple Polyps or Adenomas of the Colon

Association of Tuberculosis with Gastroenteritis

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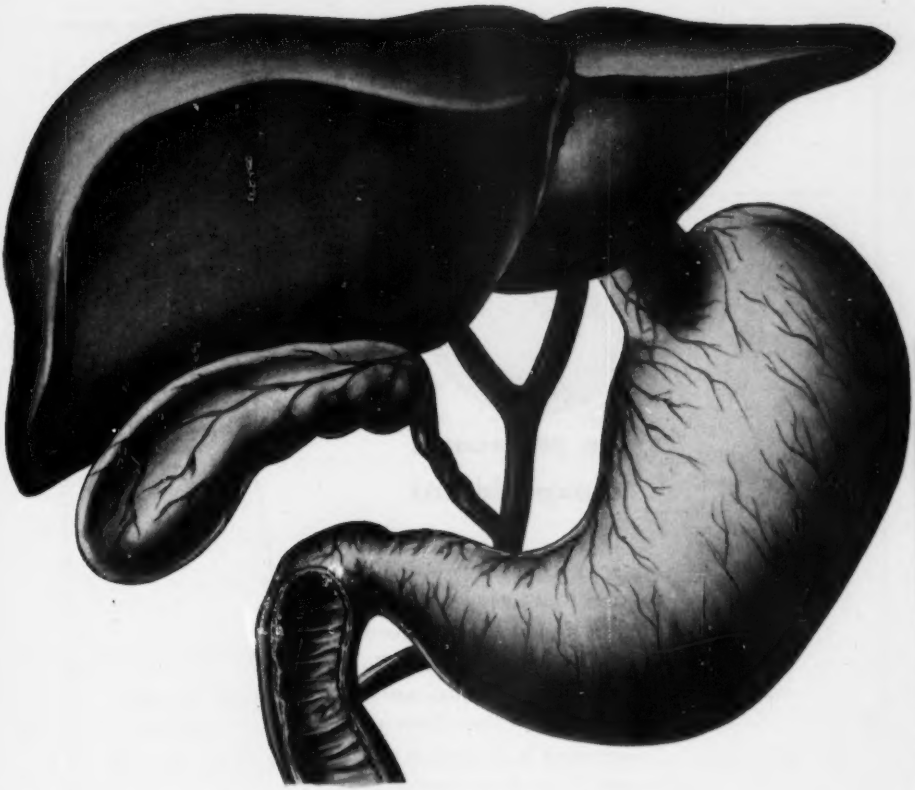

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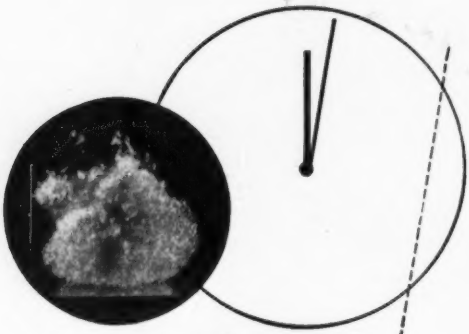

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

VOLUME 19 JANUARY, 1952 NUMBER 1

CONTENTS

Page

Editorial Board 4

General Information 6

The Use of ACTH in the Treatment of Ulcerative Colitis...*C. Wilmer Wirts, M.D. and Joseph L. Carroll, M.D.* 13

Association of Tuberculosis with Gastroenteritis.....*A. X. Rossien, M.D.* 29

The Role of the Phrenic Nerve in Vagotomy and in Gastrointestinal Mechanisms *H. Necheles, M.D., Ph.D. and N. C. Jefferson, M.D.* 39

Amebic Dysentary.....*Howard B. Shookhoff, M.D.* 48

Single and Multiple Polyps or Adenomas of the Colon and Rectum-Management.....*R. Russell Best, M.D., F.A.C.S.* 57

Hemorrhoids: Etiology, Pathology and Treatment (Part III)...*R. V. Gorsch, M.D.* 67

Editorial:

Dr. Max Einhorn—on the Ninetieth Anniversary of His Birth *Hyman I. Goldstein* 88

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Index to Advertisers

Ames Co., Inc. 12
Burton, Parsons & Co. 7
Coca-Cola Co. 87
Commercial Solvents Corp. 9
Endo Products, Inc. 8
Harrower Laboratory, Inc. 5
Hoffmann-La Roche, Inc. 2
Pfizer, Chas. & Co., The .....2nd cover, 92, 93
Robins, A. H., Co., Inc. 95
Rorer, Wm. H., Inc. 97
Schenley Laboratories, Inc. 100
Schering Corp. .....3rd cover
Searle, G. D. & Co. 1
Sentral Laboratories, Inc. 96
Upjohn Co., The 91
U. S. Treasury 98
Viobin Corp. 99
Winthrop-Stearns, Inc. 94
Wyeth, Inc. .....4th cover

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of the

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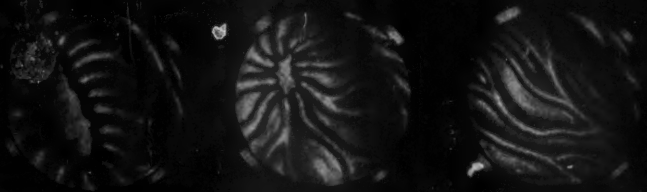

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Volume 19 JANUARY, 1952 Number 1

THE USE OF ACTH IN THE TREATMENT OF ULCERATIVE COLITIS*

C. WILMER WIRTS, M.D.†

and

JOSEPH L. CARROLL, M.D.††

Philadelphia, Pa.

A number of reports now in the literature indicate that ACTH has a beneficial effect on the course of idiopathic ulcerative colitis[1-7]. The results are best in patients who have an acute fulminating course of short duration. In these patients there is a reduction in stool frequency and volume, defervesence, improved appetite, weight gain, cessation of intestinal bleeding, correction of anemia and the development of a great sense of well being. In the majority an improvement in the proctoscopic and roentgen appearance of the bowel develops much more slowly and in some patients may show little change even though symptomatic improvement is pronounced. Remissions have been observed for periods up to 16 months and relapses are usually mild. Patients who have a long history with chronic inflammation penetrating well beneath the mucosa appear to show less response to ACTH. If they do respond favorably initially they are apt to relapse promptly when treatment is stopped.

The dosage of ACTH employed has varied widely but frequently was begun at 100 mg. to 200 mg. daily in divided intramuscular injections. Treatment was usually continued for 3 to 5 weeks and the dose gradually reduced as the patient improved. The side-effects of the drug were not frequent nor serious when the dosage was small and the treatment period brief. Massive gastrointestinal bleeding, perforated ulcer, peritonitis and severe psychical disturbances have been reported, however[8,9,10]. It appears on the basis of the available reports that ACTH has no curative effect on the underlying disease of idiopathic ulcerative colitis, but it can be a potent factor in causing a remission of symptoms.

---

*Read before the Sixteenth Annual Convention of the National Gastroenterological Association, Chicago, Ill., 17, 18, 19 September 1951.

From the Department of Medicine, the Gastrointestinal Clinic, and the Therapeutic Laboratories, Jefferson Medical College and Hospital.

†Assistant Professor of Medicine.

††McIllhenny Fellow in Gastroenterology.

Material and Methods:—We have employed ACTH in the treatment of 10 patients with ulcerative colitis and one with regional enteritis. Eight of the patients were started on ACTH (Wilson's) 20 mg. to 40 mg. intramuscularly every 12 hours. Treatment was continued for 2 to 3 weeks with a gradually reduced dose. All patients showed a positive eosinopenic effect. One patient (Case 2) who had severe chronic ulcerative colitis was given Cortisone 50 mg. (Merck) every 12 hours for two nonconsecutive two week periods and gradually tapered off. Subsequently this patient (Case 2) and another (Case 8) received ACTH 25 mg. (Armour)* every 6 hours for 2 weeks and 25 mg. every 12 hours for one week. Subsequently (Case 2) had this course of therapy repeated. One patient (Case 10) who had a good reponse to a total of 600 mg. ACTH (Wilson) and relapsed at 3 months, received 25 mg. ACTH (Armour) in 500 c.c. of 5 per cent glucose in water intravenously daily for 2 weeks. One patient (Case 11) received ACTH specially prepared for research purposes. The beginning dose was 40 mg. every 6 hours and this was gradually reduced over the next 58 days.

All cases were diagnosed by sigmoidoscopy, roentgen study or both. Similar diseases were ruled out by appropriate studies. Case 11 had amebic dysentery and ulcerative colitis. In addition to ACTH all patients were treated with the usual measures of bed rest, a high protein diet, low in salt with potassium chloride 2.0 to 6.0 gm. per day, dicalcium phosphate 2.0 gm. per day, testosterone proprionate 25 mg. daily as a protein anabolic agent, liberal amounts of vitamins, small transfusions, and in a few cases mercurial diuretics as indicated. At times several of these patients were so desperately ill that total parenteral alimentation was necessary. Antibiotics were given to 7 patients (Cases 2,3,4,5,6,8 and 11) before treatment with hormones was begun but little or no effect was demonstrable.

Case Reports

Case 1:—A. M. 27 years, male, a World War II veteran, college student was desperately ill with acute fulminating ulcerative colitis of 6 months' duration. He had lost 50 lbs., had no appetite and was having 10 or more stools per day. Bilateral polyneuritis of the lower extremities rendered his legs exquisitely tender to touch. He was unable to get out of bed and despite all antibiotics daily fever to 103-104° occurred. After 2 weeks treatment with ACTH his fever disappeared, appetite returned, he had gained 16 lbs. and was able to get out of bed (see Fig. 1). This patient has remained asymptomatic and continued to gain weight for 14 months. Due to his financial status he did not return to college but has been driving a bus for the past 5 months.

Comment:—This patient was one of the most acutely ill in our group and has had the longest remission.

*ACTH (Armour) supplied through courtesy of Harley E. Claxton, Jr., M.D., Director Medical Research, The Armour Laboratories, Chicago, Ill.

Case 2:—M. H., 53 years, male, pharmacist, was admitted in comatose state with a blood urea nitrogen of 110 mg. per cent. He had had chronic recurrent diarrhea for 25 years and immediately prior to admission had been experiencing 10-20 loose, watery stools per day. After correction of his electrolyte imbalance a diagnosis of ulcerative colitis was made. He was treated with Cortisone 50 mg. every 12 hours for 2 nonconsecutive two-week periods, after which the previous electrolyte imbalance gradually recurred and hypokalemia and hypocalcemia developed (See Fig. 2). Cortisone was therefore discontinued and symptomatic care administered. On several occasions he was unable to eat and parenteral feedings became necessary. Finally his stools diminished to 3 per day and appetite returned. After discharge he continued to convalesce at home. He gradually gained weight and strength but the stools remained loose and averaged about 3 daily. A month later he returned to work and remained in fairly good health

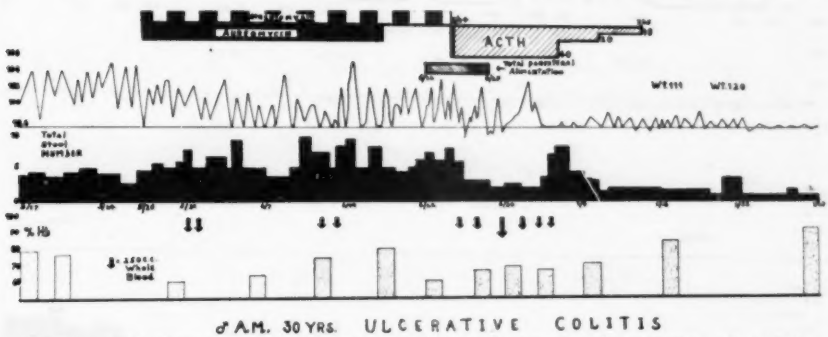


Fig. 1—Graph showing response of Case 1 before and after the administration of ACTH.

for 5 months when a severe exacerbation of diarrhea occurred. This followed a disruption with his 13 year old daughter who had a difficult time adjusting socially. There was no gross blood in the stool, appetite, weight and strength began to diminish rapidly. Since the patient was able to give himself hypodermic injections, he was supplied with ACTH and took 25 mg. every 6 hours for 2 weeks, and every 12 hours for one week. During the first week there was a decrease in stools to 1 to 2 formed movements daily and a prompt increase in appetite and weight. When the ACTH was discontinued the stools again were occasionally loose and ranged from 1 to 3 daily, but the weight gain, improved appetite and strength persisted for 2 months. At this time following a severe upper respiratory infection, another bout of diarrhea occurred and the patient passed 5 to 8 watery stools daily, he lost 5 lbs. in 10 days and anorexia developed. A second course of ACTH, 25 mg. every 6 hours was given for 2 weeks and 25 mg. every 12 hours for 1 week.

Comment:—This patient was critically ill. Not only did he fail to improve on Cortisone therapy, but the condition appeared to be aggravated. However 2 months later maximum improvement followed ACTH therapy. Relapse of mild

to moderate severity developed, when ACTH was stopped, but in spite of this he had continued to work every day as a pharmacist. At the end of 2 months he began to have severe diarrhea, moderate anorexia and weight loss. A second course of ACTH again was followed by maximum improvement which has been maintained for 3 months.

Case 3:—R. B., 28 years, male, colored, student, complained of gradually progressive diarrhea and weakness of one year's duration accompanied by a 45 lb. weight loss. He was having up to 12 stools per day. Anemia was severe with a hemoglobin of 39 per cent on admission. With transfusions, rest and ACTH appetite returned, he gained 18 lbs., hemoglobin rose to 78 per cent and stools diminished to 2 per day (see Fig. 3).

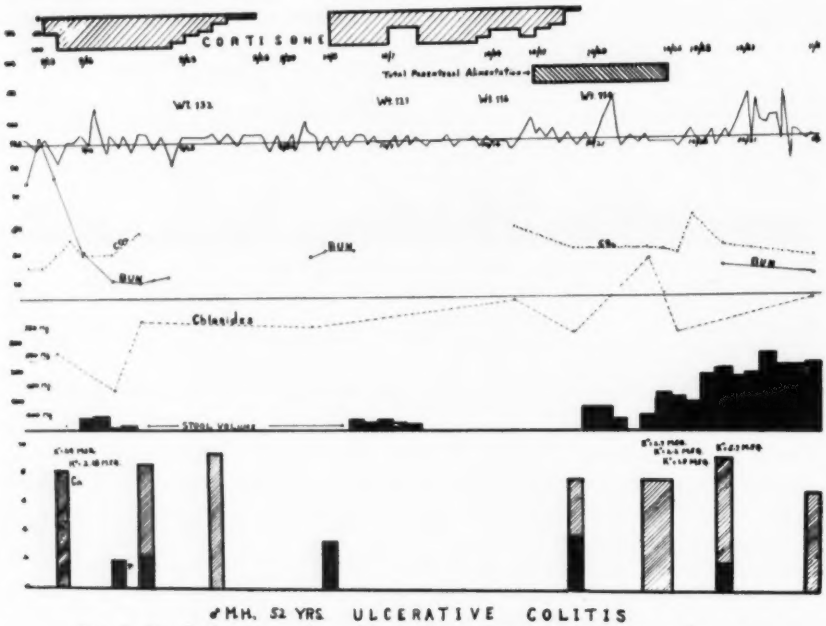


Fig. 2—Graph showing unfavorable response of Case 2 to Cortisone therapy.

Comment:—The outstanding feature of this patient's illness was the pronounced anemia. The elevated hemoglobin which followed treatment has been sustained for 10 months at a level of 88 per cent. During this time he returned to college and has been free of symptoms, except for an occasional loose bowel movement.

Case 4:—J. L., 62 years, female, seamstress, had two previous episodes diagnosed as ulcerative colitis; the first 5 years ago. There were daily temperature elevations to 102°, appetite was almost entirely absent and the patient was remote

and morose. She obviously exaggerated her complaints claiming to have had 50 to 100 stools per day. After beginning ACTH there was a striking improvement in her mood and willingness to cooperate. Appetite became ravenous and stools decreased to 2 formed movements per day (see Fig. 4).

Comment:—This patient was very depressed and incapacitated but not acutely ill. Her improvement was prompt and has continued for 9½ months. Occasionally she will have a few loose bowel movements but she returned to her dressmaking work 2 weeks after discharge and has remained on the job regularly since.

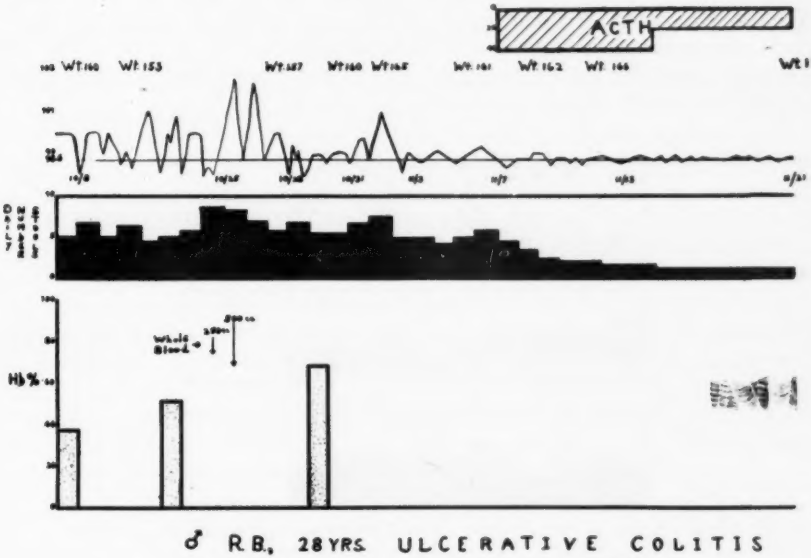


Fig. 3—Graph showing response of Case 3 to ACTH.

Case 5:—F. G., 39 years, female, housewife and hosiery-mill worker, a known case of ulcerative colitis for 6 years, experienced an exacerbation of diarrhea 5-7x with daily fever of 102-103° and painful, red, tender, swollen, ankle, knee and elbow joints. The most severe pain was in the left ankle and knee. Roentgen-ray disclosed no joint abnormality. A trial of bed rest alone and then various antibiotics failed to bring about improvement (see Fig. 5 a,b,c). At the beginning of ACTH therapy defervesence occurred and arthralgia disappeared. Stools became formed and a rather striking euphoria was observed.

Comment:—This was one of 2 patients in this group who had severe arthralgia in association with the ulcerative colitis. Bowel function has remained normal, but occasional stiffness occurs in the left knee. In general the patient is

in a good state of health 6 months after treatment and has continued the arduous duties of housekeeping for a coal miner's family of six. We have strongly advised not returning to the hosiery-mill work which she formerly did in addition to the housework.

Case 6:—G. L., 27 years, female, colored, no occupation due to illness. This patient had 3 previous admissions over a 4 year period for arthritis involving multiple joints, fever and diarrhea. No abnormalities were found in the joints on roentgen study. She had been treated once as a case of rheumatic fever and more recently as a case of rheumatoid arthritis. On this admission proctoscopy revealed idiopathic ulcerative colitis, which was confirmed by barium enema study. Fever disappeared on bed rest and antibiotics. The swollen, tender, hot joints, however, did not improve until ACTH was given when there was also a prompt cessation of diarrhea (see Fig. 6 a,b).

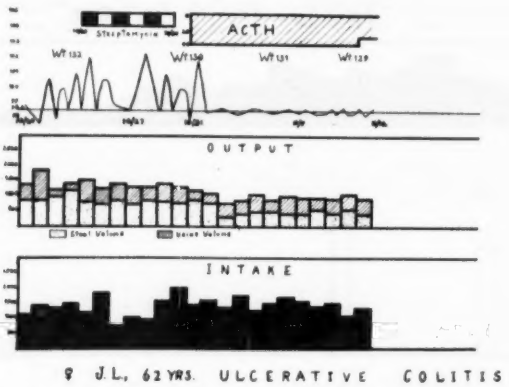


Fig. 4—Graph showing response of Case 4 to ACTH.

Comment:—This patient had been a semi-invalid for the past 4 years. Following treatment she said she felt better than at any time since the onset of her illness. Remission has continued for 7 months, except for occasional stiffness of one ankle joint.

Case 7:—F. B., 61 years, female, housewife. History of colitis for 5 years of moderate severity. Upon this admission she complained of 4 to 5 loose stools per day, streaked with blood, moderate, periumbilical, postprandial distress and a 15 lb. weight loss over a period of 6 months. She has a high strung introverted personality and had failed to respond to symptomatic therapy. Improved appetite, cessation of abdominal pain, formed stools free of blood, and weight gain followed the administration of ACTH.

Comment:—Although this patient was not acutely ill, she claimed she felt better than she had since the onset of her illness. It was the first time in the 5-year period that the stools had been formed and free of blood. Remission has continued for 5 months.

Case 8:—R. M., 24 years, male, clerk had a 4 year history of colitis with one hospital admission one year ago when roentgen study indicated involvement of the entire colon and the terminal ileum. Symptomatic treatment led to a satisfactory remission for one year. He was admitted this time because bowel movements which were formed and occurred once or twice daily were painful to pass and were always covered with streaks of blood. Proctoscopy revealed the mucosa of the terminal 6 cm. of the anorectal region to be beefy red and friable. The mucosa above this area for a distance of 20 cm. appeared only moderately congested. Five days after ACTH was started stools were passed without pain and in 10 days there was no blood in the stool.

Comment:—This patient was not acutely ill but prior to administration of ACTH 3 weeks of ambulatory treatment and 2 weeks of bed rest at home taking a bland diet, hot sitz baths and rectal oil instillations had had no ameliorating effect on the symptoms.

Case 9:—M. P., 34 years, female, unemployed due to long illness had had 11 prior admissions over a 6 year period. One ileocolostomy and 2 partial bowel resections had been performed for external and internal fistulae resulting from regional enteritis. She had never regained weight, strength or appetite since the onset of her illness 6 years ago and her stools which were liquid averaged 8 per day. All symptoms were relieved after ACTH was given; after the first week only 1-2 formed stools were passed daily.

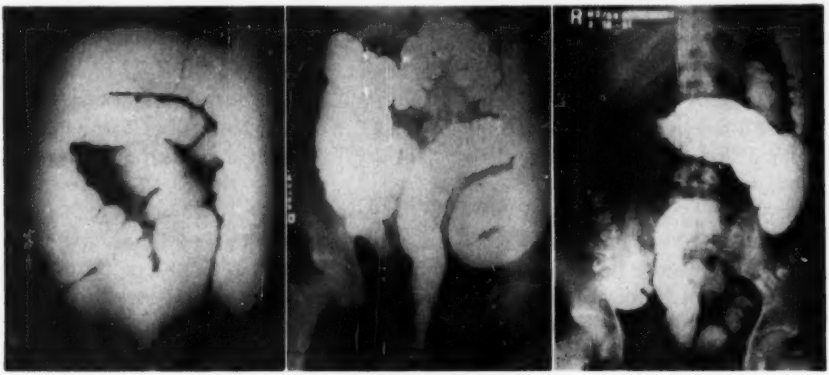
Comment:—This patient was not acutely ill but was in a state of chronic incapacitation. Now for the first time in 6 years she volunteered to take part in house duties. She has continued to have a good appetite, improved energy and normal bowel movements except for occasional loose stools for 7 months.

Case 10:—E. B., 65 years, female, housekeeper had a history of mild, chronic colitis with 2 to 3 annual exacerbations for 7 years. Recurrence of 7-8 bloody liquid stools per day began immediately after a pelvic operation for uterine fibroid. There was an associated exfoliative dermatitis involving the left lower leg, both thighs, the hands, neck and beneath both breasts. Discomfort from itching was extreme. Bed rest, modified diet and sedatives were beneficial and the symptoms somewhat relieved for 3 months. A rather pronounced relapse of the dermatitis and mild diarrhea followed the discovery that her sister had been drinking secretly and as a result was having marital difficulties. She was then given 25 mg. ACTH in 500 c.c. 5 per cent glucose intravenously over an 8 hour period daily

for 10 days and 25 mg. ACTH intramuscularly every 6 hours for 7 days. Improvement began after the first treatment. The stools were normal and were passed once daily and the dermatitis was relieved after the third day except in the left leg which did not become normal until the 10th day.

Comment:—So far this patient has had no further relapse, but it is only 2 months since treatment was stopped.

*Case 11**:—J. S. while in military service in Germany, April 1950, noted the occasional presence of bright red blood in the stool and transient diarrhea. In May 1950 about 3 weeks after discharge from the Army, bowel habit and character of stools returned to normal. For a short time he felt "a little weak and



a b c

Fig. 5—a, Roentgen ray of colon (Case 5) showing minimial change Apr. 24, 1947.
b, two years later the lesion has extended into the sigmoid.
c, almost four years later there is considerable contraction of the rectosigmoid region. No change was demonstrated in this picture following ACTH therapy.

dizzy". The patient was drafted January 19th, 1951. In early March he noted abdominal cramps, loose or watery stools, in which there was bright red blood and felt tired, sluggish and generally ill. On several occasions he had bowel incontinence.

Laboratory:—The blood count showed 3,840,000 erythrocytes, 11.5 gm. hemoglobin, 15,800 leucocytes with 84 per cent polymorphonuclear leucocytes and 15 per cent lymphocytes. Erythrocyte sedimentation rate was 29 mm/hr. corrected. The urinalysis was normal. On 13 March proctoscopic examination revealed a granular, friable mucosa for 12 cm. Gross blood gushed from the

*Case 11 was observed on the Medical Service of the USAH at Fort Dix, New Jersey and is presented through the courtesy of Col. S. J. Lerro, Chief of Medical Service, and Lt. E. K. Seiks.

TABLE I

RESPONSE TO ACTH IN TREATMENT OF ULCERATIVE COLITIS

No.	Patient	Age	Sex	Emotional State			Duration Follow-up	Weight			Stool			Hemoglobin			Appetite		
				B	A	P**		B	A	P	B	A	P	B	A	P	B	A	P
1	A. M.	27	M	−1	+3	+3	14 mos.	95	111	170	10	1	1	68	91	100	−1	+4	+4
2*	M. H.	53	M	−2	+1	+3	11 mos.	114	115	151	10–20	3	2	68	65	80	−1	+2	+3
3	R. B.	28	M	+1	+2	+2	10 mos.	153	171	165	12	2	1	39	78	88	+1	+3	+3
4	J. L.	62	F	−3	+2	+2	9½ mos.	128	133	137	+30	2	1	70	59	80	−3	+2	+2
5	F. G.	39	F	−1	+3	+3	6 mos.	152	147	153	5	1	1	78	90	71	+1	+4	+2
6	G. L.	27	F	+1	+4	+3	7 mos.	82	85	93	4	1	1–2	63	65	65	−1	+4	+3
7	F. B.	61	F	+1	+2	+3	5 mos.	112	115	119	3–4	2	1–2	85	85	85	−1	+3	+3
8	R. M.	24	M	+1	+1	+2	5 mos.	120	121	125	2	1	1	88	88	73	+1	+2	+3
9	M. P.	34	F	+1	+2	+2	7 mos.	85	92	104	8	2–1	1	73	80	91	+1	+3	+2
10*	E. B.	63	F	+1	+3	+3	5 mos.	158	157	160	4–5	1	1	88	88	90	+3	+3	+4
11*	J. S.	23	M	+1	+2	+2	7 mos.	104	125	130	10–12	3	...	50	68	...	+1	+3	...

* Figures indicate response to first course of therapy; later patients had relapse.

** B—before treatment; A—after treatment; P—present.

rectum when a repeat proctoscopy was attempted. On 29 March many cysts and trophozoites of E. histolytica were found on stool examination. The patient was therefore given aureomycin, 3 gm. daily, from 29 March to 17 April, followed by carbarsone, 0.75 gm. daily, from 17 April to 20 April inclusive and diodoquin, 4 tablets q.i.d., from 21 April to 13 May inclusive. On 23 April repeat proctoscopy showed congestion, friability and granularity of the rectal mucosa for 6 cm. and above this numerous serpiginous ulcers 0.3 cm. to 0.7 cm. in diameter with punched-out margins and white-grey bases. The impression was idiopathic chronic ulcerative colitis, severe, associated with amebic dysentery. On this same date (23 April) ACTH, 80 mg. i.m. per 24 hours was begun. Just prior to starting this medication weight was 100 lbs. and the patient showed a fever of 99° to 101°. Within 2 days the patient's appetite improved and the temperature became normal. Stools were less frequent, dropping from an average of 6 to 3 per day. The patient felt stronger and his outlook seemed more cheerful. Within a week he gained 2¼ lbs.

On 14 May proctoscopic examination showed a definite improvement over the appearance noted on 23 April, but a small perianal fistula developed after the rupture of an ischiorectal abscess. This closed spontaneously in about a month, but reopened later. Cysts of E. histolytica were again found in the stool in late June and a second course of emetine, carbarsone and diodoquin was given. No ova or parasites have been found in the stool since this time. When the ACTH was given in small amounts and finally stopped the patient's appetite fell off somewhat, he was less cheerful, and he again passed 6-8 watery stools per day.

On 20 July 1951, ACTH therapy was resumed, the drug being given in amounts of 20 mg. in 500 c.c. of glucose and water, dripped in over a period of 8 hours daily for 2 weeks. Prompt improvement was again noted and persisted to the present, one week after ACTH was stopped.

Comment:—This patient was acutely ill and suffered from both amebic dysentery and ulcerative colitis. The latter condition did not improve on amebic therapy. Instead he probably lost some ground during this period. He did improve promptly when ACTH was given, but this was interfered with when the ischiorectal abscess and perianal fistula developed. He relapsed after withdrawal of ACTH, but responded favorably when it was restarted intravenously. The second posttreatment period is too short to determine what the future course of this patient will be.

Discussion:—It appears that the favorable response in these 11 patients followed 4 to 14 months is too prompt and uniform to be purely fortuitous. As indicated in Table I, we have consistently observed during treatment (1) defervesence, (2) cessation of diarrhea with return to formed stools, (3) great increase

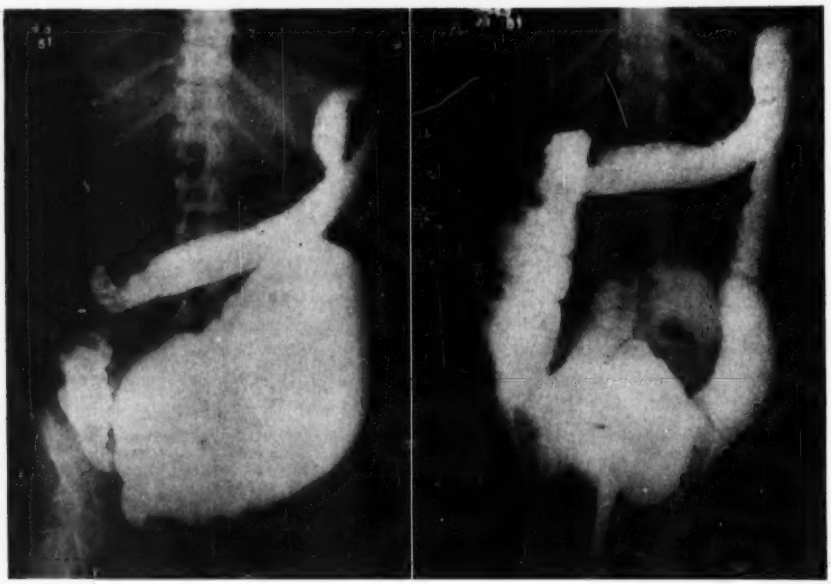
TABLE II

ULCERATIVE COLITIS

Case	Duration	Severity*	Treatment	Response	
				Immediate	Relapse
1. A. M.	6 months	+4	Dosage ACTH 20 mg. q. 12 hrs. 11 days 10 mg. q. 12 hrs. 2 days 5 mg. q. 12 hrs. 8 days total 560 mg.	excellent	none
2. M. H.	25 years	+4	Cortisone 50 mg. q. 12 hrs. 14 days total 1400 mg.	poor later improved	none
	2nd treatment period	+2	ACTH 25 mg. q. 6 hrs. 14 days 25 mg. q. 12 hrs. 7 days total 2100 mg.	good	at 3 mos.
	3rd treatment period	+2	25 mg. q. 6 hrs. 14 days 25 mg. q. 12 hrs. 7 days total 2100 mg.	good	none
3. R. B.	1 year	+2	20 mg. q. 12 hrs. 7 days 10 mg. q. 12 hrs. 7 days total 260 mg.	good	none occ. loose stool
4. J. L.	5 years	+2	20 mg. q. 12 hrs. 11 days 10 mg. q. 12 hrs. 3 days total 500 mg.	good	none occ. loose stool
5. F. G.	6 years	+3	20 mg. q. 12 hrs. 3 days 10 mg. q. 12 hrs. 10 days 5 mg. q. 12 hrs. 4 days 5 mg. q. 24 hrs. 4 days total 380 mg.	good	none
6. G. L.	4 years	+3	20 mg. q. 12 hrs. 7 days 10 mg. q. 12 hrs. 6 days 5 mg. q. 12 hrs. 3 days total 430 mg.	good	none occ. stiff joint
7. F. B.	5 years	+1	20 mg. q. 12 hrs. 14 days 10 mg. q. 12 hrs. 7 days total 720 mg	good	none
8. R. M.	4 years	+2	25 mg. q. 6 hrs. 14 days 25 mg. q. 12 hrs. 7 days total 1750 mg.	good	none
9. M. P.	6 years	+2	40 mg. q. 12 hrs. 7 days 20 mg. q. 12 hrs. 10 days 10 mg. q. 12 hrs. 3 days total 1020 mg.	good	none occ. loose stool
10. E. B.	7 years	+2	20 mg. q. 12 hrs. 3 days 20 mg. q. 6 hrs. 5 days 20 mg. q. 12 hrs. 2 days total 600 mg.	fair	3 mos.
	2nd treatment period	+3	25 mg. i.v. daily 10 days 25 mg. q. 6 hrs. 7 days total 825 mg.	good	none
11. J. S.	5 years	+4	20 mg. q. 6 hrs. 14 days 10 mg. q. 6 hrs. 14 days 10 mg. q. 12 hrs. 14 days 10 mg. q. 24 hrs. 14 days total 2100 mg.	fair	during treatment
	2nd treatment period		20 mg. i.v. daily 14 days total 240 mg.	good	none

* +4—Acutely ill; +3—severely ill; +2—moderately ill; +1—mildly ill.

in appetite which was formerly one of the most difficult aspects to overcome, (4) improvement in the depressed, negativistic emotional state which is so characteristic of patients with this disease, (5) weight gain which usually increases after discontinuation of treatment, and (6) correction of anemia. Proctoscopic appearance of the bowel regularly showed some degree of improvement but usually several weeks after relief of subjective symptoms had occurred. The amount and persistence of this was quite variable. Roentgen study by barium



a b

Fig. 6—Roentgen view (Case 6)

a, Jan. 29, 1951, showing involvement of ascending and transverse colon, the large opaque mass in the lower left quadrant is redundant sigmoid.
b, one month after ACTH therapy, showing some improvement in the ascending and transverse colon.

enema was not regularly performed; improvement in the mucosal pattern was reported in one patient (Case 6) but usually a change was hard to distinguish.

In evaluating the favorable response to treatment in these patients it is important to note the length of time they had colitis and the severity of their disease as indicated in Table II. It will be noted that 3 patients (Cases 1, 2, 11) were acutely ill, 2 patients (Cases 5, 6) were severely ill, 5 patients (Cases 3, 4, 8, 9 and 10) were moderately ill and 1 patient (Case 7) was mildly ill. In this regard it appears worthy of comment that one of our sickest patients (Case 1)

had the most dramatic response, has had no relapse in 14 months and has been working as a bus driver for the past 5 months. The second seriously ill patient (Case 2) failed to respond to Cortisone but responded later to 2 courses of ACTH given while he was ambulatory and working. He has shown the greatest weight gain (37 lbs.) over a period of 7 months. A second relapse of a milder character responded to a second course of therapy.

While no complications resulting from ACTH therapy itself occurred in these patients a number had associated diseases that played an important part in the course of their illness. One patient (Case 1) had a *perianal fistula* 0.5 cm. in diameter prior to administration of ACTH. This has changed little since. The patient has no symptoms from it but surgical treatment is contemplated. Another patient (Case 11) developed a perianal fistula during ACTH therapy but after discharging for one week closed spontaneously; later it reopened. *Arthritis*, sufficiently severe to prevent walking in 2 patients (Cases 5 and 6) was promptly relieved by ACTH and has not recurred. However both patients noticed occasional mild stiffness in one ankle joint. One patient (Case 10) had severe *exfoliative dermatitis* of the left leg, both thighs, both hands, the face and beneath both breasts. This was relieved by ACTH, recurred rather promptly following a severe emotional disturbance, but responded to a second course of ACTH, on this occasion given intravenously. One patient (Case 3) had a severe *anemia*. The hemoglobin which was 39 per cent rose to 88 per cent after ACTH therapy and has remained at this level to the present, 10 months following treatment.

Relapse has been noted in Case 2 on two separate occasions but favorable response followed 2 additional courses of ACTH. At present, 3 months after the last course of therapy he maintained his weight, appetite and strength. The stools occur once or twice daily and are occasionally loose. During their periods of observation 3 patients (Cases 3, 4 and 9) had occasional loose stools and one patient (Case 6) had occasional slight stiffness in one ankle. Case 10 had a mild recurrence of diarrhea and a severe recurrence of exfoliated dermatitis. This responded to ACTH given intravenously. Case 11 showed moderate relapse while receiving small doses of ACTH following development of a perianal fistula but a good response was obtained after the intravenous administration of the hormone. All patients, but one (Case 11) have resumed their normal duties.

Conclusions:—From this study ACTH appears to be a potent form of adjunct therapy in the treatment of idiopathic ulcerative colitis. Previously recognized forms of therapy are still necessary and should be used as clinical judgment dictates.

Remission of the colitis can occur up to 14 months, but we do not feel that the underlying disease is cured, because no patients have shown a complete return to a normal proctoscopic appearance of the bowel. Also many patients

continue to have some abnormality in bowel function and relapse may still occur in any of them. Emotional disturbance, upper respiratory infection or complications such as fistula formation may cause relapse, just as it does in patients not treated with this hormone. Such relapse may be treated with good results in some patients by repeating the course of ACTH. We have observed no side-effects from the use of ACTH in this group of patients except the development of moderate rounding of the face giving it a moon-like appearance.

It appears that doses as small as 20 mg. ACTH every 12 hours intramuscularly for 2 to 3 weeks may be sufficient to cause a cessation of symptoms. If improvement is not noted in 48 to 72 hours the dose should be increased when given intramuscularly, or the intravenous route may be tried. It is desirable to use the smallest effective dose to avoid side-effects and reduce expense.

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Discussion

Dr. Joseph B. Kirsner (Chicago, Ill.):—Dr. Wirts has given us a very conservative analysis of a rather difficult subject. As you know, the natural history of ulcerative colitis is characterized by "spontaneous" remissions and exacerbations, and this tendency must be taken into consideration in evaluating any new therapy. In general, our experience at the University of Chicago coincides with that of Dr. Wirts and Dr. Carroll. We have now had the opportunity to treat, over a period of about two years, approximately fifty patients with chronic ulcerative colitis, the majority classified as severe; all had not responded consistently to a variety of therapeutic measures.

In this study, control observations were obtained with saline solution or distilled water, dispensed from ACTH-labeled bottles; transitions from the

placebo to the hormone were made without the knowledge of the patient. Other adrenal substances also were employed as controls; none of these preparations had any demonstrable beneficial effect upon the course of the disease.

The improvement has been as described by Dr. Wirts; one of the most striking, of course, was the great emotional upsurge and sense of well-being. I might add parenthetically that ACTH, and perhaps Cortisone to a lesser degree, may conceal the overt manifestations of an emotional disorder, but it does not dissolve the conflict; the emotional stresses tend to persist and probably are responsible for many recurrences of the disease.

A variety of objective measurements of clinical response has been utilized, including 24-hour fecal outputs and the concentration of lysozyme in the feces. The output of fecal nitrogen decreased, paralleling similar trends in the fecal weight and lysozyme. In one patient the level of nonspecific hyaluronidase in the serum declined in a manner similar to that described for rheumatic fever. The erythrocyte cholinesterase is increased during the active stage of ulcerative colitis and diminished during improvement with ACTH, as observed also with other forms of therapy. It is important to note that the improvement was no more complete with ACTH than has been observed in its absence, but it seems to be more rapid.

Our experience with long-acting ACTH has not been striking thus far, but newer, more potent preparations may be more useful.

ACTH intravenously has been of definite value in partients not responding to the standard method of administration; 20 mg. of ACTH have been administered in 500 c.c. of 5 per cent dextrose in distilled water, injected slowly over a period of eight to ten hours; effective adrenocortical stimulation was obtained, as judged by the eosinophile counts.

The matter of relapses has been properly emphasized by Dr. Wirts, and I can only reemphasize this observation. ACTH does not cure ulcerative colitis, although the clinical remission may be prolonged. On the basis of present evidence, it seems apparent ACTH does not eliminate the basic cause or causes of the disease. However, in conjunction with other established therapy, the management of the problem has been somewhat easier and an unfavorable trend may be reversed. ACTH or cortisone should be regarded as adjunct therapy; it should be given only under conditions permitting very careful clinical and laboratory control of the patient. The concurrent administration of sulfonamides and antibiotics is advisable to prevent or decrease the tendency to suppurative complications, although this has not been a major problem in our experience thus far.

The nature of the ACTH-induced remissions is not yet known; both specific and nonspecific mechanisms may be involved. This phase of the problem has

been of special interest to me because we now have an additional tool for the study of the disease; properly used, it may provide us with important new information concerning the pathogenesis of ulcerative colitis.

Dr. C. J. Tidmarsh (Montreal, Canada):—I think Dr. Wirts mentioned he had tried ACTH in one case of regional ileitis. I should like to ask him whether he thinks it is going to be effectual in that disorder as well as ulcerative colitis.

Dr. C. Wilmer Wirts (Philadelphia, Pa.):—In answer to Dr. Tidmarsh's question, the patient we treated with regional enteritis had an eight-year history. No procedures carried out before admission to the hospital were therapeutically effective. In no instance after admission was her response to symptomatic care good or as long lasting as it was with ACTH therapy. Her course since adding this form of treatment has been good. She still has occasional loose stools, but she had had no bouts of fever, and no severe diarrhea over this period of eight months.

One patient is hardly sufficient upon which to draw conclusions, but I think ACTH should be tried in regional enteritis because of the great similarity of the disease to ulcerative colitis.

I want to thank Dr. Kirsner for his remarks and I am certainly stimulated to find that his large series of patients are showing results that are favorable.

We have now treated five patients using the hormone intravenously and found the response just as prompt and the required period of treatment somewhat shorter when compared to the intramuscular administration. Of course, the saving of expense to the patient is an additional advantage. Consequently we expect to give this form of therapy additional trial.

ASSOCIATION OF TUBERCULOSIS WITH GASTROENTERITIS*†

The Problems of the Gastroenterologist in Tuberculosis

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A succinct presentation of the subject, which would at the same time be all inclusive, is impossible. The subject, however, merits considerable attention since a tuberculous patient cannot and will not respond to treatment without a well functioning gastrointestinal tract. The patients' nutrition must be maintained otherwise all other treatment loses its maximum affect. It is not enough to expect that the gastroenterologist become tuberculosis conscious; the pulmonary tuberculosis specialist must become gastrointestinal conscious. Best results

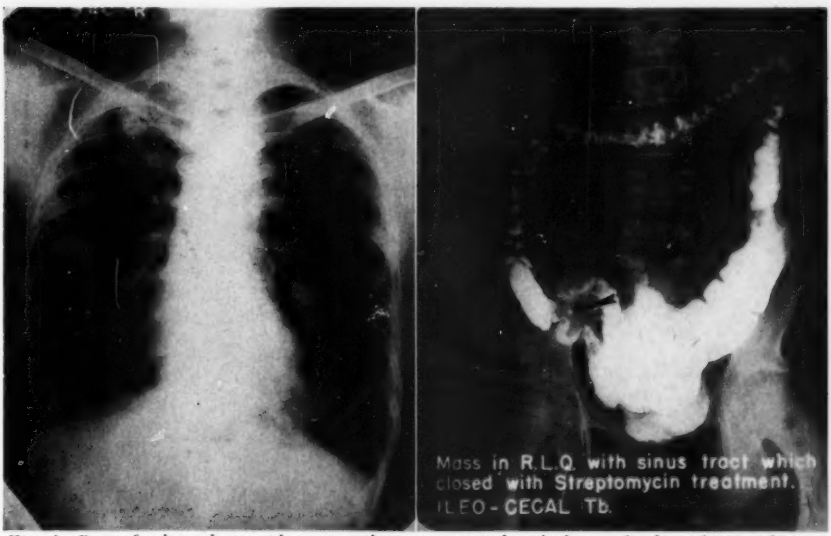

Fig. 1—Case of tuberculosis with pneumothorax associated with ileocecal tuberculosis and sinus tract formation. The sinus tract closed with streptomycin treatment.

may be expected only when there is coordination in the treatment outlined by those in charge of these two specialties—they must supplement each other.

Primary Tuberculous Enteritis

Tuberculosis of the digestive tract in this country may, for all practical purposes, be considered as always being secondary to pulmonary tuberculosis.

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*Read before the Sixteenth Annual Convention of the National Gastroenterological Association, Chicago, Ill., 17, 18, 19 September 1951.

†From the Department of Medicine (Dr. Richard H. Bennett, Medical Director), Division of Gastroenterology (Dr. A. X. Rossien, Visiting Gastroenterologist) of Triboro Tuberculosis Hospital, Jamaica, New York.

Primary tuberculous gastroenteritis is practically extinct in the United States, thanks to the public health regulations which demand periodic routine cattle examinations, pasteurization and certification of milk and also health certification of food handlers. Prior to these regulations the ingestion of milk infected with bovine tubercle bacilli was a relatively frequent source of infection which resulted in primary tuberculous enteritis of children. It is also conceivable that kissing pulmonary tuberculosis patients and contamination by tuberculous food handlers could be other sources of primary tuberculous enteritis.

In this disease the initial lesion is in the intestinal wall, but due to the tendency to rapid healing of the thereby formed minute primary ulcers, these ulcers may not be macroscopically observed at autopsy. Therefore, it is generally ac-

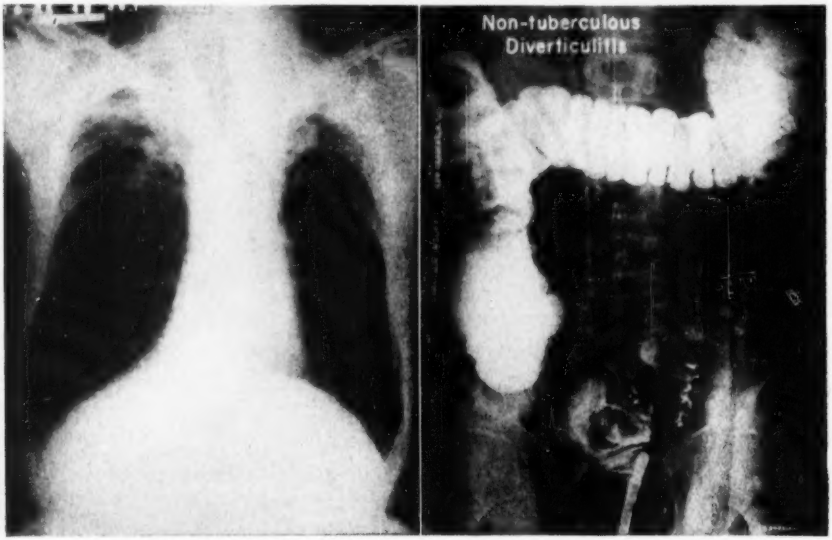

Fig. 2—Patient with advanced pulmonary tuberculosis with associated non-tuberculous chronic obstructing diverticulitis proven at operation and laboratory section of tissue.

cepted that the presence of tuberculous mesenteric nodes, without evidence of tuberculosis elsewhere, implies that the original lesion was in the intestinal wall.

A diffuse ulcerative involvement of the intestines is comparatively rare in primary tuberculous enteritis. A tumor mass in the ileocecal region may be present. This mass cannot roentgenologically be differentiated from other neoplasms. Laparotomy and biopsy afford the only means of differentiation at the present time. The diagnosis of primary tuberculous enteritis should be made only when there is no involvement of other organs and when the bacteriologic and histopathologic criteria are fulfilled.

Secondary Tuberculosis of the Digestive Tract

Tuberculosis of the digestive tract, as previously mentioned, is practically always secondary. Dysphagia may be due to tuberculous lesions of the hypopharynx, larynx, epiglottis and less frequently of the esophagus. Obstruction by a tuberculous lesion of the esophagus is not common. Mediastinal lymph nodes may adhere to the esophagus and thereby cause traction diverticulae. These may rupture into the left bronchus and produce fistulae.

Gastric tuberculosis is very rare[2,3] probably because the mucous membrane is resistant or the tubercle bacilli cannot take hold in the presence of the mixture of pepsin, renin and hydrochloric acid. Further, gastric peristalsis normally propels the stomach contents along its path within six hours. Gastric peptic ulcers may develop in patients with pulmonary tuberculosis provided that the patient does not have an achylia gastrica. However, protracted pulmonary tuberculosis, not unlike most chronic wasting diseases, frequently is accompanied by an atrophic gastritis with an anacidity.

The most frequent digestive tract complication of pulmonary tuberculosis is tuberculous enteritis, which usually starts in the terminal ileum. The bacilli are swallowed with the sputum and after passing through the intestinal mucosa reveal their affinity for lymphoid tissue by invading Peyer's patches and solitary lymph follicles. While the involvement may remain local, the tendency is for the usual processes of ulceration to take place. These ulcers usually encircle the bowel because that is the route of the lymph channels. These ulcers present ragged undermined edges. The process of ulceration is slow thereby giving ample time for adhesions to form between loops of intestine and to contiguous structures. This accounts for the low incidence of perforation. An accompanying endarteritis obliterans of the smaller arteries explains the infrequent occurrence of hemorrhage as a complication.

Approximately 70 per cent of chronic pulmonary tuberculous patients present autopsy evidence of ulcerative tuberculous enteritis. Patients having laryngeal tuberculosis have an even higher incidence, approaching about 90 per cent[4].

Gastroenterologist's Problem

The problems of the gastroenterologist in tuberculosis hospitals are usually divided into distinct parts, namely; the diagnosis and treatment of the patients and secondly the opportunity to thoroughly investigate the patients.

At the present time it may be said that it is impossible to lay down one diagnostic syndrome of gastrointestinal tuberculosis. Further, I know of no criterion whereby this disease can clinically be positively diagnosed without the knowledge that the patient had or has tuberculosis elsewhere, particularly of the lungs.

The finding of tubercle bacilli in the gastric contents and/or the feces is not *ipso facto* gastrointestinal tuberculosis. The x-ray findings, in spite of some of the reports in the literature[5], are not pathognomonic of this disease. Gastrointestinal functional disorders are frequent developments in pulmonary tuberculosis patients and may have a fatigue and/or toxic basis without being accompanied by actual tuberculous gastroenteritis.

Further, a pulmonary tuberculous patient is subject to all of the other illnesses that may affect other humans. His gastrointestinal symptoms may be due to associated gastrointestinal lesions varying from hiatus hernia, gallstones with chronic cholecystitis, gastritis, regional ileitis, peptic ulcer, carcinoma, idiopathic ulcerative colitis, amebiasis, infectious hepatitis, diverticulitis and to many other

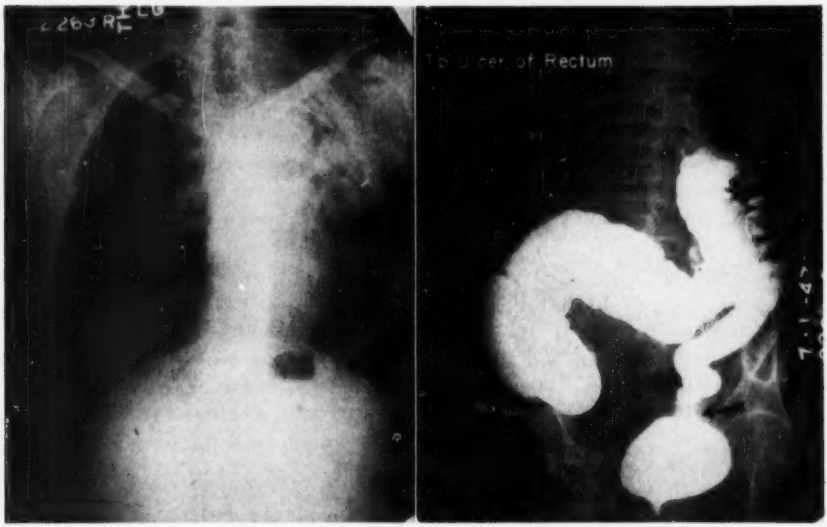

Fig. 3—Case of advanced diffused pulmonary tuberculosis with associated laboratory confirmed tuberculous ulcer of the rectum, without other evidence of tuberculosis of the gastrointestinal tract.

lesions of the digestive tract. Most of these we have seen at the Triboro Tuberculosis Hospital.

There is a need for gastroenterological services in tuberculosis hospitals to be given every opportunity for thorough investigation of the patients.

Diagnosis

Healed or active chronic pulmonary tuberculous patients who experience anorexia, diarrhea and abdominal pain warrant our special attention as those

most likely to have tuberculous gastroenteritis. This is particularly true if the patient was progressively improving and developed a sudden temperature rise which was irregular or if the patient started on a downward course.

Ulceration of the bowels must be suspected when sudden and continued diarrhea develops, particularly following the ingestion of rough or raw foods or cold liquids.

Fear of eating because of subsequent or exaggerated existing cramp-like pain in the lower mid-abdomen or the right lower quadrant is strongly indicative of gastroenteritis. Should the pain become worse, persistent and localized and accompanied by a temperature rise with nausea and vomiting, there is great likelihood that an ulcer is penetrating and peritoneal irritation has developed.

Fig. 4—Patient with advanced pulmonary tuberculosis complicated by hepatomegaly due to infectious hepatitis with jaundice. Silent gallstones were present which at operation were shown not to obstruct the biliary tract.

The finding of tubercle bacilli in the feces is only of slight diagnostic significance. Macroscopic blood in the feces is uncommon due to the endarteritis obliterans previously mentioned. When present it is likewise of slight diagnostic significance.

X-ray studies are important adjuncts but not definitive in the diagnosis of this disease. Segmentation and dilatation of the small intestines, a string-like sign at the ileocecal juncture, barium in the terminal ileum on a 9 hour study, a poorly outlined cecum with a reasonably well outlined ileum and ascending colon

and/or a completely visualized colon at 12 hours that becomes practically completely empty at 24 hours are significant and may be considered as suggestive of tuberculous enteritis in healed or active cases of pulmonary or other known existing tuberculosis.

One must not, however, lose sight of the fact that regional ileitis, amebic colitis, enteritis, carcinoma, idiopathic ulcerative colitis, functional gastrointestinal disorders and allergy may give a part or all of the x-ray pictures described and may coexist with tuberculous gastroenteritis.

Treatment

The treatment of tuberculous gastroenteritis is dependent almost entirely on the treatment of the practically always prexisting pulmonary tuberculosis. It is beyond the province of this presentation to outline the treatment for pulmonary tuberculosis. Institution of treatment for any of the aforementioned possible associated conditions is likewise essential lest they interfere with recovery from the pulmonary involvement by depletion of the patient's general health. Ultraviolet ray exposures to the abdomen, low roughage and high caloric with high vitamin diet, symptomatic medicinal relief and, where necessary, psychotherapy in conjunction with the pulmonary treatment, merit trial.

To date streptomycin has given us some promising clinical results. However, the clinical picture is not confirmed by favorable x-ray changes. Further, the clinical improvements seem to be only temporary. However, tuberculosis sinuses do heal and remain closed.

Intravenous alimentation has given us favorable results in diarrhea cases only during the period of its administration. The diarrhea returned almost immediately after treatment was stopped.

Gastroenterological Investigations

The gastroenterologist's investigations in a tuberculosis institution are in direct proportion to the opportunities that the specialists of pulmonary tuberculosis make available to him. It is difficult to appreciate the necessity of awaiting a gastroenterological consultation request in a tuberculosis institution.

The multiplicity of gastrointestinal problems of a pulmonary tuberculosis patient are so varied and frequent that the gastroenterologist's opinions, studies and treatment should be made available to the patient without the formalities usually practiced. It is urgently essential to give recognition to the fact that the pulmonary tuberculosis specialist can receive added information from the gastroenterologist in like proportion to the degree of service that the gastroenterologist performs. While the gastroenterologist must become tuberculosis conscious, the pulmonary tuberculosis specialist must become "gastrointestinal conscious". We cannot permit ourselves the luxury to forget that—and this is not to appear

facetious—a patient may have ingrown toenails and curly hair at one and the same time.

The patient's nutrition must be maintained if his pulmonary lesion is to be healed regardless of the type of direct chest treatment that is instituted.

Summary

An effort was made to succinctly present the diagnosis and treatment of tuberculous gastroenteritis. The multiplicity of gastrointestinal lesions that could be and frequently are associated with pulmonary tuberculosis was enumerated. The importance of maintaining the patient's nutritional processes through the cooperation between the gastroenterologist and the pulmonary tuberculosis specialist was reiterated.

Conclusion

There is still much to be investigated in the study of tuberculosis.

Since "*Satis magnum alter alteri theatrum summus*" is still valid, we should all have the opportunity to play our respective part towards our goal,—healing the tuberculous patient and preventing the spread of this disease.

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Discussion

Dr. Elihu Katz (New York, N. Y.):—Dr. Rossien's paper is of extreme interest to those who are affiliated with a tuberculosis hospital. He stresses the importance of the coexistence of pulmonary tuberculosis and gastroenteritis, and the troublesome digestive disturbances which occur with pulmonary tuberculosis. Every specialist in medicine naturally considers his department the most important, and, it is reasonable to infer that in a tuberculosis hospital, the chest specialist should claim preeminence. However, in pulmonary tuberculosis, the gastroenterologist believes his specialty to be of considerable importance. One of the chief reasons for this is that the gastrointestinal tract is frequently affected by pulmonary tuberculosis from the aspirated tubercle bacilli of the sputum and their toxic substances. Patients suffering from pulmonary tuberculosis may also have coincidental nontuberculosis disease of the gastrointestinal tract. Furthermore, to secure adequate nutrition in the patients affilicted with pulmonary

tuberculosis, perfect digestion is essential. This means a structurally and functionally normal gastrointestinal tract. Establishing a correct gastrointestinal diagnosis and instituting proper therapy are the problems of the gastroenterologist.

At Seaview Hospital for Pulmonary Tuberculosis, with a bed capacity of over 2,000, every patient admitted into the hospital has in addition to the routine work-up, a complete gastrointestinal survey to determine the presence of intestinal tuberculosis. In doing this, such disorders as gallbladder disease with and without stones, esophageal lesions, and other nontuberculous gastrointestinal disturbances as those mentioned by Dr. Rossien, are often discovered. Mindful of this fact that patients with pulmonary tuberculosis are subject to all diseases of the gastrointestinal tract, the gastroenterologist, in ruling out the presence of ileocecal tuberculosis, often encounters many unsuspected pathological conditions.

Dr. Rossien divided intestinal tuberculosis into two groups, primary, and secondary. In our clinical classification, intestinal tuberculosis is divided into four groups. 1) Primary, more frequently observed in the Pediatrics Service, and rarely in adults. When present in adults, it is of the hyperplastic type, and may cause obstruction necessitating surgical intervention. 2) Secondary intestinal tuberculosis, which is one of the most common complications of pulmonary tuberculosis. It begins as an ileocecal lesion, and spreads upwards and downwards on either side of the ileocecal sphincter. 3) So-called independent ileocecal tuberculosis, in which the lesion in the chest cavity progresses favorably, and may go on to complete healing, while, the ileocecal lesion shows progression of the disease. In spite of all therapy, the ileocecal lesion steadily continues with increasing malnutrition and asthenia to a fatal termination; and, lastly, 4) Rectal tuberculosis, which is characterized by fistula formation. In this group, the pulmonary lesion may go on to arrest with negative sputum, but the fistulous tract remains, and careful search may reveal tubercle bacilli.

The diagnosis of gastrointestinal lesions, tuberculous, or otherwise, in patients with pulmonary tuberculosis, is established by the usual procedures employed in a gastroenterological work-up. These include a complete history, physical examination, clinical laboratory and roentgenographic studies, and other special procedures as may be indicated. Should gastrointestinal symptoms at any time appear in the patient afflicted with pumonary tuberculosis, the immediate problem is to exclude tuberculous ileocecal enteritis. In this, the history is important. It is difficult to determine when the ileocecal lesion actually starts, its onset being so insidious. When the ileocecal tuberculosis does occur, it usually appears within two years after the onset of the pulmonary lesion. As Dr. Rossien pointed out, the first indication of its presence may be a change in temperature without a change in the lung findings or symptoms. A change in

the patient's temperament may be the first indication of the presence of ileocecal tuberculosis. Continued loss of weight that cannot be explained by the pulmonary lesion, should make one suspect ileocecal tuberculosis.

A characteristic symptom which aids in diagnosis is pain of varying intensity in the lower right abdominal quadrant usually appearing about the time when the gastrocolic reflex occurs. This characteristic pain occurring about twenty minutes after a meal may indicate ileocecal tuberculosis. It is due to peritoneal irritation from the enlarged tuberculous glands upon contraction of the cecum. It also accounts for the tenderness frequently found in the lower right quadrant. Vomiting, diarrhea, and, in fact, any change in the usual gastrointestinal symptoms of a patient afflicted with pulmonary tuberculosis, may suggest the presence of an ileocecal enteritis.

The next problem is to confirm the diagnosis. In doing this, roentgenography is the most important procedure. It is essentially by this study that other nontuberculous gastrointestinal lesions are usually discovered. It is important therefore, that every patient with pulmonary tuberculosis should have complete gastrointestinal roentgenographic studies, both by the oral method, and by the injection of the opaque enema. Roentgenographically, gastrointestinal motor dysfunction, especially hypermotility and spasticity, are significant of tuberculosis. These may be the only initial findings to suggest the presence of tuberculosis (Stierlin phenomena). As the disease develops, other roentgenographic changes characteristic of gastrointestinal tuberculosis may be observed.

Dr. Rossien has demonstrated several nontuberculous gastrointestinal lesions coexisting with pulmonary tuberculosis. I should like to call attention to the frequency of peptic ulcer accompanying chronic pulmonary tuberculosis. It is not unusual to discover a peptic ulcer even when the pulmonary pathology is far advanced. Roentgenography reveals a crater or niche, and the gastric analysis discloses a hyperacidity. Such ulcers are known to exist with or without ileocecal tuberculosis.

Another condition that may co-exist with pulmonary tuberculosis is terminal ileitis. Not infrequently, young patients are admitted to the hospital with terminal ileitis and pulmonary tuberculosis. The differential diagnosis between this disease and ileocecal tuberculosis is often difficult. In terminal ileitis, the lesion usually stops at the ileocecal sphincter, while, in tuberculosis, the structural changes are on either side of it. The irregularity of the cecum is due to the external pressure caused by the enlarged glands, whereas, in intestinal tuberculosis, the irregularity is due to the lesion itself which at the same time is present in the ileum.

Dr. Rossien should be congratulated upon his excellent presentation, and the National Gastroenterological Association complimented for the opportunity

given to him to call attention not only to the problems of the gastroenterologist in chronic pulmonary tuberculosis, but, to the importance of correct gastrointestinal diagnosis and proper therapy.

Dr. A. X. Rossien (*Kew Gardens, N. Y.*):—I want to thank Dr. Katz for his remarks and express appreciation for some of the additional information he has given. The time is getting short and the next speaker is due. I want to say one more thing and close.

I felt a little hesitant in presenting this particular paper before this august body particularly because you are men interested in and limiting most of your practice to the field of gastroenterology. Nevertheless, how can we expect the attention of the pulmonary specialist to be given to the gastrointestinal tract to the degree that we would like to see it, if we do not bestir ourselves to call their attention to the importance of that tract and the fact that the nutritional processes must be kept in good condition in order for their treatment readily to take effect in the healing of the tuberculosis patient!

THE ROLE OF THE PHRENIC NERVE IN VAGOTOMY AND IN GASTROINTESTINAL MECHANISMS*

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and
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Laboratory Experiments

Our interest in the relationship between the left phrenic nerve and gastrointestinal mechanisms was aroused by an early experiment in which we tried to produce peptic ulcer in the dog[1]. An anastomosis was made between the central end of the left phrenic nerve and the distal stump of the left vagus nerve. It was thought that the constant discharge of respiratory impulses from the phrenic into the vagus and then into the stomach would lead to constant irritation similar to that which is thought to produce peptic ulcer in man. In the first dog that was operated in this manner, 10 months after operation, acute dilatation of the stomach occurred and the animal died from throttling of the venous return to the heart. Upon immediate autopsy, about 10 ulcers were found surrounding the cardia, in a tremendously dilated stomach, which had pushed aside all other organs in the abdominal cavity. Such a result was not obtained subsequently in a series of dogs subjected to the same anastomotic operation. However, it was found that within 18 to 20 months a functioning anastomosis had formed between the left phrenic and vagus nerves, with nerve fibres going from the phrenic into the vagus. In acute experiments, stimulation of the phrenic nerve above the anastomosis was followed by distinct contractions of the stomach. However, physiologically, respiratory impulses did not produce changes in the appearance or in kymograph balloon records of the stomach. The animals subjected to this operation were fluoroscoped at regular intervals in order to study the effect of the beginning of functioning of the nerve anastomosis, i.e., we expected to find rhythmic contractions of the stomach from the respiratory center. This was never observed, confirming the acute experiment described above. However, it was noted that the emptying time of the stomach was shortened considerably following interruption of the left phrenic nerve. For this reason, a number of chronic experiments were performed in which only the left phrenic nerve was sectioned in the dog, between the hilus of the lungs and the diaphragm. All animals were operated under aseptic conditions and received antibiotics following the operation. After recovery, gastric emptying time was determined at regular intervals up to 20 months using a standard barium meal[2].

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Section of the left phrenic nerve in the dog had a distinct effect on emptying time of the stomach, shortening it between 20 and 60 per cent, with an average of 30 per cent. The possible mechanism of this fast emptying of the stomach can be demonstrated in x-ray pictures, which demonstrate a considerable change in position of the stomach following left phrenicotomy[2]. The left diaphragm moves up high into the chest and the stomach follows it. By this moving up of the stomach, the axis between cardia and pylorus is straightened out and also the angle of the duodenum in relation to the stomach is flattened.

Autopsy or biopsy showed that the musculature of the left diaphragm had atrophied completely within 14-20 months, except when an occasional aberrant branch of the phrenic nerve had not been sectioned at operation. In that case, we have found that half of the diaphragm was completely atrophied and half of it had a normal appearance and contracted with every respiration. It has been claimed by thoracic surgeons and phtisiologists that section of the left phrenic nerve abolishes respiratory movements of the diaphragm on the left side only for a limited period of time, and that the function of the phrenic nerve is taken over by lumbar and by sympathetic nerves. These auxiliary nerves are supposed to conduct the respiratory impulse to the diaphragm which thus regains its respiratory function. From our experiences on many dogs, we do not believe that this can occur. If the phrenic nerve has been interrupted, and the diaphragm has been replaced by fibrous and fatty tissue, no nerve impulse can make muscle fibres in the diaphragm to reappear. Therefore, if respiratory function is still observed after section of the phrenic nerve, it must be due, in our experience, to either one of two reasons. Either an acessory branch has been overlooked, and fluoroscopically the diaphragm gives the appearance of normal respiration, or regeneration of the phrenic nerve has occurred. In the dog, it took 3 to 6 months for regeneration of the phrenic nerve and recovery of the function of the diaphragm[3]. However, we know that in the dog, after 14 to 20 months, regeneration of the phrenic nerve cannot reactivate a degenerated diaphragm[4].

In man, a gastrocardiac symptom-complex has been described to follow exeresis of the left phrenic nerve, and has been called "Roemheld's Syndrome". The symptoms consist of cardiovascular and gastrointestinal disturbances. Bradycardia and premature systoles, tachycardia, vertigo, anxiety, epigastric distress, lack of appetite, nausea, vomiting and eructations were observed. We have observed our animals with left phrenicotomy for the objective manifestations of Roemheld's syndrome, but have not been able to find any[2]. We believe with Noack[2], that occurrence of such symptoms as enumerated above is due to tearing of and trauma to sympathetic fibres during exeresis of the phrenic nerve in the neck.

We have performed many vagotomies in the dog. Bilateral vagotomy just below the hilus of the lungs leads to severe symptoms. The stomach distends

greatly, occupying most of the abdominal cavity and contains mostly air. This air seems to be aspirated through the esophagus and may be related to the continuous vomiting and to relaxation of the cardia. Actually, the vomiting often seems to be more a spilling-over of stomach contents than actual vomiting. Some animals vomited for weeks and months, and their state of nutrition became exceedingly bad. Gastric retention was of such a high degree that little of the food was evacuated into the intestine. Intravenous nutrition had to be given, partly also to prevent dehydration and loss of crystalloid substances in the vomitus.

It was natural that we should apply our experience with interruption of the left phrenic nerve to these doubly vagotomized animals with dilatation of the stomach and constant vomiting. For this reason, a series of dogs was operated, both vagi were sectioned, as described above, and the left phrenic nerve was also sectioned. In this series of animals, no vomiting occurred, the food left the stomach within a very short period of time, and the dogs appeared practically normal. The only difference that could be seen between normal dogs and dogs in whom the above operation had been performed, was that the stomach was high in the left chest, and that the air bubble in the fundus was relatively large. However, the air bubble did not seem to impair the motility and emptying of the stomach. No ulcers, or serious disturbances were noted in the stomach or in the intestine of this series of animals. We concluded, therefore, that the adverse effects of section of both vagus nerves on the stomach of the dog could be overcome by section of the left phrenic nerve[2].

In our work on vagotomy in the dog, we felt that complete interruption of the vagus supply to the stomach could *not* be achieved either by supra- nor by infradiaphragmatic vagotomy. Too many filaments of the vagus nerve enter the musculature of the esophagus and run inside of it into the stomach. In addition to that, short branches of the vagus nerve enter the esophagus and establish synaptic connections with its intrinsic plexuses; the latter are contiguous with those of the stomach. Therefore, vagus activity can be transmitted through the intact esophagus in the absence of external vagus nerves. Furthermore, vagus fibres run into the celiac ganglion and from that ganglion go to the stomach with the sympathetic fibres along blood vessels. It is possible that these connecting branches are not cut during vagotomy. A further question is the possibility of the outflow of parasympathetic or rather cholinergic fibres from the spinal cord, which may go with the sympathetic fibres along the blood vessels. We, therefore, were led to believe that nervous shock from the handling and the sectioning of the vagus fibres leads to atony of the stomach and loss of secretory function, as well. This was tested in a simple control experiment in the dog. The left chest was opened and all visible vagus fibres were elevated gently with a smooth hook and separated for a distance of about 2 centimeters from the esophagus. Following this, they were dropped and the incision was closed as usual. We do not

believe that the manipulation of the vagus fibres destroyed their blood supply or their viability. In this animal, a profound dilatation of the stomach occurred just as seen following double vagotomy, lasting for 5 months after the operation, when the animal was sacrificed. A large atonic stomach was found at autopsy, and the vagus fibres were grossly intact. Further work on this interesting observation is continued in our laboratory[5].

The above observation is in line with observations of surgeons in man, where incomplete section of the vagus nerve has, in a number of cases, led to atony of the stomach, disappearance of the ulcer distress of the patient, and healing of the ulcer. It is also confirmed by observations that, in a number of incomplete vagotomies where the insulin test still indicated existence of vagus fibres to the stomach, atony of the stomach was present and the clinical results were good. We, therefore, feel that the beneficial effects which vagotomy may give are due to a profound nervous shock and atony of the stomach by which the ulcer pain disappears. The logical consequence of this observation would be that the results of vagotomy for prevention of ulcer cannot be permanent. We realize that this assumption can be criticized on various grounds by a number of opposed observations, yet we feel it worthwhile to let our results be known and to do further work along these lines.

During our studies of bilateral vagotomy in the dog, cardiospasm was observed in a number of animals[5]. We felt that this was due to interruption of the vagus supply and this belief is supported by animal experiments and by a few observations in man, where cardiospasm followed vagotomy for ulcer. We had noted previously that in none of the phrenicotomized dogs and in none of the vagotomized and phrenicotomized dogs a disturbance of the cardia was seen. Therefore, the effect of left phrenicotomy on the cardia was studied in the dog and we found that it did not produce cardiospasm and that it was able to overcome the cardiospasm often following bilateral vagotomy.

It was natural that we should have studied the effects of right phrenic section on the gastrointestinal tract. The right diaphragm went up high, pulling up the liver and the gastrohepatic ligaments. We have never seen a pylorus that high in the dog. The physiological effects of this change on the position of the liver, the gallbladder, the common duct, the pylorus, and the first part of the duodenum, is being studied.

Experiences in Man

It was natural that we should apply some of the results gained from experiments in dogs in the practice of surgery in man[6]. A number of our patients that had been vagotomized in the treatment of peptic ulcer showed serious symptoms of retention, vomiting and distention of the stomach, although a gastroenter-

ostomy had been performed, together with the vagotomy. So far, in 6 patients a double infradiaphragmatic vagotomy, gastroenterostomy, and left phrenic crush has been performed, with excellent results. The left phrenic nerve was dissected and crushed in the neck by one surgeon, while vagotomy and gastroenterostomy were done by another team. The operation on the phrenic nerve took only 15 to 20 minutes, and was relatively atraumatic. The patients were out of bed on the first day after operation; none of them vomited, none of them had distention, their stomachs emptied in a short period of time, and they were all back to work within a few weeks after operation. X-ray pictures of these patients before and after operation demonstrated that the stomach moved up into the left chest. Gastric emptying times were as short as 15 minutes, an unusually short time in a patient with bilateral vagotomy. In this series of operations, Dr. U. Dailey, chief surgeon of Provident Hospital, led the way and without his courage, initiative and help, we could not have obtained results in man as quickly, as efficiently, and as well controlled.

While we were doing this work at Provident Hospital, a patient with hiccups of several months duration, was brought in and none of the known modes of therapy could give relief. His doctor thought that something desperate, like fracture of a bone should be done in order to stop these hiccups. However, it was decided to do a phrenic crush in this patient. The left phrenic was crushed first and, while the number of hiccups per minute were reduced, they continued without letup. Therefore, it was decided to crush the right phrenic immediately. This was followed by complete cessation of hiccups and by well-being of the patient, who was discharged from the hospital the next day. No respiratory distress was noted by this patient; however, we did not subject him to any particular effort which, we believe, would have produced shortness of breath.

The next case that came to the hospital was also of interest. It was an old lady of 74 years of age with a bad heart and with a large diaphragmatic hiatus hernia, which produced pain and hemorrhage. In view of the cardiac condition of this patient, a major operation was considered to be too dangerous. Therefore, the left phrenic nerve was crushed. The patient lost her distress immediately and has been free of symptoms now for more than 2 years. An x-ray film demonstrated that the hernia had receded considerably. It has not disappeared completely, probably because of adhesions. However, the relaxation of the diaphragm seems to be sufficient to relieve pressure and congestion, and it has prevented, up to now, further hemorrhage, distress, or ulcer formation.

The next group of patients in which we intended to use left side phrenic interruption for treatment naturally was cardiospasm. Our results in the dog had encouraged us so much that one of our group, Dr. Clyde Phillips, operating at the Freedmen's Hospital, in Washington, D.C., undertook this operation in a patient who had been suffering from cardiospasm for the last 5 years. The condition in this patient was believed to be true achalasia of the cardiac sphincter

of the stomach. A crush of the left phrenic nerve in the neck was performed, and the results were entirely gratifying. The patient has lost the cardiospasm, is able to eat without any disturbance, and has regained his weight within a few weeks.

In summary, we can state that section of phrenic nerve has profound effects on gastrointestinal mechanisms:

1. It shortens the emptying time of the stomach, probably by raising the stomach so that the axis between cardia and pylorus is straightened out.
2. Right phrenic section raises the pylorus, the liver, the gallbladder and the bile ducts considerably.
3. The disturbing effects of vagotomy as used in the treatment of peptic ulcer, in man, can be overcome by crushing the left phrenic nerve in the neck.
4. The profound atony of the stomach, which is usually seen following bilateral vagotomy, can be produced also by simple lifting of the vagus nerves in the chest of the dog. It is possible that the atony and decrease of the function of the stomach following vagotomy are not due so much to section of the vagus nerves, but to a profound shock into which the stomach is put by manipulation or by trauma to vagus fibres.
5. Hiccups can be interrupted in man by crushing of both phrenic nerves in the neck.
6. Cardiospasm which may follow vagotomy, or cardiospasm by itself, can be overcome by left phrenic section or crush of the left phrenic nerve in the neck.

Our experimental and surgical results also carry with them a moral. If our results obtained were proved to be of value in surgery in man, we have to thank the dog for this. Without animal experimentation, we would not have dared to add interruption of the phrenic nerve to vagotomy. We would not have dared to do a bilateral phrenicotomy for hiccup. We would not have thought of using left phrenic crush in the treatment of cardiospasm. And, if the further interpretation of our laboratory results will be of use, like our observations on vagotomy-like effects of handling of the vagus nerve in the chest of the dog, we have to thank again this experimental animal. I want to appeal to you to do everything you can to support the universities, the medical schools, and the research institutes in their fight against antivivisection. It is understood, of course, that none of us ever thinks of inflicting pain or cruelty on an animal.

Another notion which we have from the work of our group, is the value of close cooperation of experimentalists, clinicians, and surgeons. Undoubtedly, we would not have been able to apply our results in such a short time and in such a

convincing manner to human therapy if it had not been for the interest and the cooperation in the laboratory of a group of good surgeons. Particularly in a private hospital, where more applied than academic research is being done, this cooperation shows that not only fruitful results can be obtained, but that both parts can profit from their mutual experiences.

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Discussion

Dr. N. C. Jefferson (Chicago, Ill.):—I can verify what Dr. Necheles has just reported to you, both in the experimental animal and in man. I have done part of both phases of this work.

We did not study the effects of phrenicotomy on the chest or on the lungs because much has been written in the past in that respect. Essentially, the anatomical distribution of both phrenic nerves in man and in the dog are similar. On the left side the distribution in the diaphragm is in three divisions, anterior, lateral, and posterior, whereas on the right side the distribution in the diaphragm is anterior and posterior. The third branch goes through the diaphragm and to the celiac plexus; from there, fibres go to the liver, and what they do there, we are in the process of studying.

Very definitely, the effect of phrenicotomy in cases of cardiospasm should be better in man than in animals, because the extrinsic circular sphincteric fibres around the esophageal hilus are more developed in the human than in the animal. At a recent meeting I was asked whether I had ever seen rupture of the diaphragm from one of these permanently denervated diaphragms which had degenerated into fibrous tissue and fat. We have not seen such. The reason may be

that our patients had no pulmonary tuberculosis and they did not cough or did not cough very much. That may be part of the explanation. I can visualize how, if a person would cough a great deal with such a weakened sheath of fibrous tissue and fat from a permanently denervated diaphragm, he might rupture it.

An important item in denervation of a diaphragm is, whether you want to interrupt the phrenic nerve permanently, or only temporarily. We believe that you cannot assure yourself of permanent interruption of a phrenic nerve in the neck in the human, and that the only way to do it is to cut it in the chest. In the case of treatment of cardiospasm this may be necessary.

Dr. Clyde W. Phillips (Washington, D. C.):—Dr. Necheles has already summarized the cases of cardiospasm that we have had the opportunity to do in Washington at Freedmen's Hospital. We have seen three cases since December 1950, first a fifty-eight year old female with a five-year history of cardiospasm proven by esophagography and diagnostic esophagoscopy. We performed a temporary left phrenic nerve interruption on the patient and she had remission of symptomatology for approximately three months. At that time she began to have obstructive difficulty concomitant with reactivation of the left diaphragm. We decided to perform a permanent interruption, a left phrenicotomy was done and the patient is now approximately six months postoperative without any difficulty.

Our second case was a rather dramatic one, in a young male thirty-four years of age, who gave an eighteen-month history of cardiospasm which had responded previously to dilatation; however, this patient had been negligent in attendance at the gastrointestinal clinic and at the time we saw him he weighed approximately 89 pounds and was in a markedly malnourished condition. We performed left phrenicotomy on this patient and during the operative procedure the patient was able to tell us that he felt relief from the full sensation that he had experienced substernally and at the cardia. This patient began to eat on the afternoon of operation and within two weeks' time had gained approximately fifteen pounds. We saw him just before leaving Washington last week, and his weight was up to 125 pounds; he was completely without symptomatology except for occasional regurgitation of water.

Our third patient is a young male student at Howard University, aged twenty-three years, who had been cognizant of difficulty in swallowing solids particularly, and also liquids since the age of fifteen. This patient had been picked up by mass survey at the university. A mediastinal mass was demonstrated and upon giving him barium to swallow a tremendously dilated esophagus was seen. We attempted esophagoscopy, but his retention of approximately twelve hours prevented complete visualization of the cardia. This patient also received a permanent left phrenic nerve interruption. We saw him just before

leaving Washington and he was approximately three weeks postoperative without having experienced any difficulty in swallowing food. Previously it had been necessary for him to employ voluntary pressure methods, increasing his endothoracic pressure in order to empty his esophagus. At night he experienced regurgitation and choking spells as the retained contents poured back and spilled over into his tracheobronchial tree.

We have had the opportunity to give all of these people thick and thin barium mixtures and observe the barium pass very rapidly along the cardia, into the stomach and on past the lesser curvature into the duodenum, as opposed to the preoperative visualization during which we had seen the barium bolus come down to the cardia and become obstructed.

AMEBIC DYSENTERY*

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In this brief discussion of amebic infections, it shall be my purpose to do two things: first, to bring to your attention some present-day concepts concerning clinical manifestations and laboratory diagnosis, and second, to present some views and observations on therapy, old and new.

Clinical Manifestations

I feel somewhat critical of myself for having accepted, in deference to popular usage, the title "Amebic Dysentery". I should prefer, and should have requested, "Amebiasis". Most of us who are actively engaged in the study of Endameba histolytica infections have come to use the latter term, because the former conveys a distorted concept of the clinical picture. "Dysentery" is descriptive of only a small minority of cases, sufficiently severe or advanced so that bloody diarrhea dominates the picture. Actually, amebiasis is now recognized as a chronic infection of the colon which gives rise to constitutional and nervous manifestations as well as gastrointestinal disturbances, and which is characterized by periodic exacerbations which may be brief or prolonged, mild or severe.

It is not generally recognized just how insidious amebic infections may be. It is often asserted that the majority of infected individuals have no symptoms. I believe, however, that the asymptomatic carrier is much less frequent than surveys seem to show. When such asymptomatic carriers, found through routine stool examinations, are given specific therapy, it is not unusual to have them return and state that they feel better. These patients recognize their symptoms only after specific therapy has produced unexpected improvement in health.

Some infected individuals will complain only of rather vague symptoms such as chronic fatigue, dizziness, mild epigastric distress, or headache or a combination of such symptoms. In such patients, physical examination is usually negative, and blood counts, sedimentation rates, chest x-rays, and other routine tests are usually normal. Very often the next step is the psychiatrist's couch. These two groups of patients, those with vague symptoms, and those whose symptoms are recognized only after treatment, have been aptly described by Craig[1] as carriers with symptoms.

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In those patients in whom the symptoms of amebiasis are more definite, diarrhea is not necessarily one of them. In our experience, it is absent in one-third of symptomatic cases. In children, abdominal pain is more frequent than diarrhea. Other relatively frequent gastrointestinal manifestations are constipation, flatulence, abdominal distress, anorexia and nausea. Pruritus ani is occasionally due to amebiasis.

Among the constitutional symptoms, fatigue is the most frequent. Others are arthralgia, backache, low-grade fever, and anemia. The nervous symptoms include nervousness, headache, dizziness, irritability, and depression.

It is quite true that many of the symptoms I have mentioned are vague. Most of them are commonplace and can be caused by a variety of disease states. No combination of them is at all diagnostic of amebic infection. The point is that patients with vague ill-defined symptoms should be studied for amebiasis, just as they are studied for tuberculosis, diabetes, syphilis, brucellosis, and neurosis.

Laboratory Diagnosis

With rare exceptions, the diagnosis of amebiasis is made in the laboratory. It is made by the technician who is not afraid of, and who is adequately trained in, examination of stool specimens with the compound microscope. Expert examination of properly obtained stool specimens cannot be replaced by sigmoidoscopic examinations, radiologic studies, or serological tests, much as one might prefer these more esthetic procedures. The therapeutic test is only infrequently justified and must be carried out with the greatest of skepticism and critical judgment.

In my opinion some students of the dysenteries have over-emphasized the value of the sigmoidoscope in the diagnosis of amebic infections. Lesions within reach of the sigmoidoscope occur in only a minority of cases. My experience agrees with that published by Klatskin[2] and Spellberg and Zivin[3], who worked with service and ex-service personnel. The former found mucosal changes in not more than one-third of cases, the latter in only 31 of 85 cases. Even in those cases which show lesions, the pathology is often not classical. The picture observed may simulate exactly that of chronic ulcerative colitis.

Specimens obtained through the sigmoidoscope may be of great value in bacillary dysentery, but in my experience with amebiasis they may be disappointing and confusing. They are certainly less satisfactory than the examination of fresh, diarrheal stools.

I do not mean to suggest that your patients should not be sigmoidoscoped. Even if Endameba histolytica has been demonstrated in the stools, thorough

study of the colon both by radiologic methods and by direct vision is frequently indicated to discover coincidental conditions such as hemorrhoids, polyps, or carcinoma, or complications such as stricture or so-called ameboma. And if lesions due to amebiasis are present, it will be important to observe them after therapy to help determine whether the treatment has been adequate.

For the definitive diagnosis of amebiasis, there is no substitute for adequate examination of the stools. Given a properly trained parasitologist, there must still be cooperation between the clinician, the patient, and the laboratory if an adequate yield of positive results is to be obtained. The examination should include one or more warm, freshly passed, diarrheal stools. It is true that, at times, one can find cysts in a formed specimen which may be one or two days old. But in infected individuals cysts may be formed in an irregular manner so that there are often periods of one or more weeks when there are no cysts in feces, or at least, not a sufficient number to be detected even by concentration methods. It is also true that, if a stool specimen is brought to the laboratory within an hour or two after it is passed, trophozoites may be found on direct examination or after culture, provided of course, that the technician does not put it aside for more important—or more esthetic—work, such as blood counts. But the best results in the shortest time will be obtained by the examination of diarrheal stools carried out promptly after the stool is passed.

Those patients who do not have diarrhea at the time of the laboratory examination must be given a saline cathartic. In order that the diarrheal stool may be promptly examined, it is necessary to bring the patient to the laboratory. This is more easily done with outpatients than with hospital patients. Even our best hospitals may lack the proper provision for this type of examination. If, as is usually the case, the specimen must be transported by an attendant, there is frequently sufficient delay to render the examination unsatisfactory or useless.

The value of warm, postcathartic stools as opposed to casual specimens is shown by the following figures:

During a period of eight consecutive months, we were able to establish the diagnosis of Endameba histolytica infection in 293 individuals. In 250 of these, we were able to obtain casual specimens and examine them by the zinc sulfate concentration method. The study of a single specimen by this technic showed E. histolytica in only 43 or one-sixth of the total cases. On the other hand, fresh diarrheal specimens were tested in 282 individuals of this group. E. histolytica could be found in the first diarrheal specimen in 208 or four-fifths of those eventually demonstrated to be infected.

It is, of course, possible to culture E. histolytica. Not all strains grow easily, and, in actual laboratory practice, the culture is not a substitute for direct examination, but an auxiliary method.

Complement-Fixation Reaction

We are just completing a study of the clinical value of the complement-fixation test in amebiasis. We have now submitted specimens on almost 300 cases to one or more of four different laboratories. While the test needs further refinement, and it is true that results tend to vary from one laboratory to another, we feel that the procedure is of definite, although limited, value. We agree with Hussy and Brown[4] that it is of value in diagnosing some cases of amebic hepatitis and liver abscess. It cannot be used to diagnose intestinal amebiasis, because it is negative in almost all such cases unless there is also hepatic involvement. Even when hepatic involvement is present, a negative test may be obtained. In other words, a negative result proves nothing, but a positive is usually significant, and points to hepatic involvement.

Hepatitis

It is not generally appreciated that hepatitis may occur in amebiasis without necessarily leading to abscess formation. English language textbooks do not describe the recurrent, subacute, and chronic forms of amebic hepatitis, although they are receiving increasing attention in the periodical literature.

Symptoms suggestive of low-grade hepatitis include nausea, especially in the morning, marked fatigue, and lack of appetite, or capricious appetite. Pain over the liver is as often absent as present. On the other hand, the majority show tenderness over the liver. Various chemical disturbances such as a positive cephalin flocculation test, indicative of hepatitis, may be observed, but they are not constant or characteristic.

Therapy

We are indeed in a fortunate position with respect to the therapy of amebiasis as compared with physicians of the previous generation. Thirty years ago, only emetine was available. Now we have a wide and ever-widening array of specifics. In fact, we have so many that it has become somewhat difficult to choose the drug or drugs to be used in any given case. The specifics on the market and in general use in this country are:

Emetine hydrochloride

Arsenical compounds
- Carbarsone
- Milibis

Iodine-Quinoline compounds
- Anayodin or Chiniofon
- Diodoquin
- Vioform

Chloroquine (Aralen)

Antibiotics
- Aureomycin
- Terramycin
- Bacitracin

In addition, the sulfonamides and penicillin, and possibly streptomycin, while not amebicidal, may be valuable adjuncts in therapy.

I am not at all sure what is the best treatment for amebiasis. Recent articles on the subject usually present dogmatically a system of therapy, with no concrete evidence that it is better than any other. Certainly not all cases deserve or require the same treatment. In general, cases with well-marked symptoms will require more intensive treatment. Carriers and mild cases will often respond to the administration of a single oral amebicide, such as Diodoquin or carbarsone. But generalizations in this respect are dangerous; sometimes mild, chronic cases are more difficult to cure than severe and relatively acute infections.

We lack adequate data upon which to judge the comparative value of the various amebicides. There are a number of reasons for this. One is the absence of long-term follow-up studies, due partly to indifference on the part of the profession. Another is the technical inadequacy in many studies of the laboratory examinations. A third is the variation of the severity of the disease in different groups of cases. When the average case in a treated group is mild, the results will be better than when it is severe.

At the Tropical Disease Diagnostic Service we are attempting to obtain comparative data by analyzing and re-examining more than 750 cases of amebiasis seen during the last six years. The collection and compilation of such data is a long and tedious operation. Our present and preliminary impression is that in intestinal amebiasis, carbarsone, Diodoquin, aureomycin, Milibis, Vioform, and terramycin are all reasonably effective. The last three appear to be a little less so than the first three. Chiniofon is less satisfactory and bacitracin still less so. Chloroquine fails in the majority of intestinal cases but is excellent for hepatic complications.

It must be emphasized that there will still be exceptions in individual cases. For example, I have one patient in whom Diodoquin, aureomycin, Aralen, and carbarsone failed, and Vioform effected a cure. There is a reported case in which bacitracin was successful where the combination of carbarsone, Diodoquin, Aralen (chloroquine diphosphate) and aureomycin[5] had failed.

None of the therapeutic agents mentioned is 100 per cent effective; each has a margin of failure. Consequently, it seems reasonable to use combinations of drugs, usually given in succession rather than simultaneously.

One might use, as many practitioners do, an iodine compound like Diodoquin, followed after a short interval, by an arsenical like carbarsone. Or one might combine an antibiotic with either drug. Our knowledge of the relative value of these therapeutic combinations is even less satisfactory than that of indi-

vidual drugs. In my opinion, efforts of clinical investigators should be concentrated on this problem.

I should like to comment briefly on the various specifics.

Emetine:—Of emetine, it can be said that "The more you use it, the less you use it". It is a very toxic drug. Aside from its cardiovascular effects, it often makes the patient feel worse than the amebic infection. A graduate nurse recently commented on her experience with it by saying, "It took me quite a while to get over the treatment".

There is general agreement that emetine alone is inadequate therapy. Craig[1] states that 80 per cent of cases so treated will relapse. I know of no convincing evidence that the combination of emetine injections with any of the oral amebicides gives a higher rate of cure than the oral amebicide alone. Therefore, I do not use it routinely, except where there is severe diarrhea or liver involvement.

Some teachers are still handing down the idea that one must give emetine to eliminate the amebae in the tissues while the oral amebicide is killing the cysts. This is a most unrealistic dogma. Cysts are formed from trophozoites; they do not reproduce themselves. If all trophozoites were killed, no cysts would be formed. Therefore, emetine should be sufficient therapy by itself, but it is not. On the other hand, many cases are cured with oral amebicides alone; these agents must and do have an action on the trophozoites. *In vitro* observations confirm this. Finally, there is no evidence that cysts affect the individual in whose intestine they are formed; they are pathogenic only when ingested. So, as cysts, they do not require treatment.

I shall not recite the toxic effects of emetine, which you can find in any text. It is usually recommended that the patient be kept at bed rest during emetine therapy because of the toxic effects on the heart. At the end of treatment he is allowed up. This is not entirely logical, since emetine is slowly excreted and its toxic effects persist after administration is stopped. Furthermore, the cardiac effects of emetine may not occur until as long as three weeks after the completion of therapy[6]. If bed rest is indicated, it should be continued for four weeks. Since four weeks of bed rest is now known to have deleterious effects of its own, I prefer to keep the patient semiambulatory if he requires emetine. He is not permitted to work and allowed only a minimum of physical activity. This is continued for a period of four weeks.

Iodine-Quinoline Compounds:—Among the iodine-containing compounds, Diodoquin seems the most satisfactory. Side-effects, with the exception of anal irritation, are infrequent, and rarely important. Diarrhea and abdominal pain occur only rarely. Vioform appears equally free of undesirable qualities but

somewhat less effective in the recommended dose of 0.25 gm. three times a day. Anayodin or Chiniofon is very prone to produce diarrhea. In full doses of 1.0 gm. three times a day, it almost never fails to do so. Perhaps because of this it is not adequately taken in many cases; in any case, its therapeutic usefulness is less than that of Diodoquin.

Arsenicals:—In adults, on the basis of short-term study, Milibis seems equal in effectiveness to the older carbarsone. However, in the reduced dosage used in children, carbarsone is superior. With carbarsone, diarrhea is a relatively common side-effect, but it usually does not interfere with giving full doses. We have seen none of the serious manifestations of arsenical toxicity. The recommended dose of 0.25 gm. twice a day for an adult is probably too small for best results. We are using 0.25 gm. three times a day.

Antibiotics:—Recently, there has been great interest in the use of antibiotics, especially those given orally, in amebiasis. Since time is short, and I have summarized the subject in a recent article[7], I shall not discuss these in detail. Aureomycin and terramycin are definitely effective. Bacitracin is effective but relapses are frequent. Chloramphenicol is not useful. Penicillin is often effective symptomatically and in conjunction with iodine or arsenical compounds. Aside from the possible therapeutic value of these agents, it is important to realize that their tentative use before stool examinations are ordered will interfere greatly with the laboratory diagnosis. This is so not only of aureomycin, terramycin, and bacitracin, but also of penicillin and incidentally, the sulfonamides.

Chloroquine:—The adaptation of chloroquine to the treatment of hepatic amebiasis is one of the outstanding advances in therapy of the last ten years[8]. This drug, which is known by the trade name of Aralen, is certainly as good as emetine and much less toxic. In certain cases of liver abscess refractory to emetine, it has proven effective. Basnuevo and his colleagues[9] have clearly demonstrated that Aralen can replace emetine in conjunction with the operative therapy of amebic abscess.

In acute hepatitis without abscess Aralen appears very satsifactory. My own experience has been largely with its use in subacute and chronic hepatitis. In these cases the effects of Aralen treatment are not as dramatic as in acute cases, but the same can be said of emetine therapy. However, it is rare not to observe some degree of improvement when Aralen is given in cases of low grade amebic hepatitis.

While less toxic than emetine, Aralen does have troublesome side-effects at times. These are anorexia and nausea, interference with visual accommodation, and occasionally marked psychic stimulation which may require interruption of therapy.

Much more could be said on the subject of therapy, but I should like to conclude with an exhortation. I urge you to be critical in evaluating reports of the effectiveness of amebicides. Don't make haste to use the new remedy while it still cures. Compare it with the results of known amebicides. As a sort of standard, let me offer you some preliminary figures obtained by us in surveying our therapeutic results with Diodoquin. Of 80 consecutive adults treated with Diodoquin, stool examinations, carried out one to two months following completion of therapy were negative in all but two cases. These examinations included fresh, postcathartic specimens, and so constituted a more severe test of effectiveness than casual specimens. Longer follow-up revealed three additional failures, one of which had received grossly inadequate doses. As judged by stool examinations, this gives a cure rate of over 90 per cent. Therefore, working with the type of amebiasis we see in the northern United States, a new drug must have close to 100 per cent effectiveness to make a better showing than those already in use. This fact is often overlooked, and claims of 70 and 80 per cent effectiveness are presented as remarkable results.

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Discussion

Dr. Frank C. Val Dez (Chicago, Ill.):—I should like to thank you for the privilege of being here to talk and discuss this paper, particularly because I think you will agree with me that it was an excellent discussion of the subject, a subject that is almost impossible to cover in twenty minutes.

It was particularly interesting to hear Dr. Shookhoff call our attention to the fact that dysentery is not necessarily amebiasis. I think over a period of many years we have thought of amebiasis only when a dysentery was present. He has reiterated to us the fact that dysentery is a symptom of amebiasis and not necessarily diagnostic.

His calling our attention to the symptoms and findings that might be present in amebiasis is again particularly good. It probably, when taken as a whole, will be the cause of our investigating these patients more completely for the presence of amebiasis; then very likely we will make the diagnosis more frequently.

The Chicago area has been rather fortunate in the last ten or fifteen years in having an ample amount of cases to study for amebiasis, and I think most of us here would conclude, that probably previous to that time we had been a little negligent in looking for the presence of amebae as a cause of illness.

The therapeutics involved in the treatment of amebiasis, excepting the antibiotics are quite old. In my own experience I have more or less, stuck to the iodine and arsenic preparations, and they have given very good results; however, I think I should call your attention to the fact that it is not the primary treatment of amebiasis that gives you the end result over a period of years. It is the check-ups. I have had an unusual number of recurrences after a series of arsenic preparations and following those with a series of iodine preparations, so it has become my custom to check the patients every six months regardless of how well they feel or what their complaints are. I think you will be surprised to find the number of recurrences that you have.

Antibiotics are, as you know, new medications, and yield very spectacular results in most of the things for which they are chosen. They relieve the symptoms of many diseases and I wonder if that may not be the case with amebiasis. My experience with them has not been extensive, but that has been my experience in the cases in which I have used them. They have given me excellent immediate results, but they have not maintained those results over a period of years.

If I may go back and say a few words about the diagnosis of amebiasis, it would be to say and to reiterate just what Dr. Shookhoff has said, that examination of the stools is the crux of the diagnosis. A therapeutic treatment of amebiasis on the basis of a history and physical is not satisfactory, and in order to avoid that, you must examine the stools, because that is the final thing that makes the diagnosis for us.

Dr. Howard B. Shookhoff (New York, N. Y.):—I should like to apologize if I spoke too rapidly, but I was trying to cover a good deal of ground. There is no doubt that the longer the follow-up period, the more treatment failures one observes in amebiasis. In my opinion we should not be satisfied with anything less than a one year follow-up period in evaluating a therapeutic regimen.

SINGLE AND MULTIPLE POLYPS OR ADENOMAS OF THE COLON AND RECTUM—MANAGEMENT*

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The clinical finding of single or multiple polyps or adenomas in the colon and rectum will not be unusual to the internist, general practitioner or surgeon provided he has a proctoscope available, uses it frequently, and requests barium enema studies with the air contrast technic frequently. The terminology for this subject to be discussed is a little confusing because "polyp" is a gross anatomic term describing a growth with a pedicle and "adenoma" refers to a glandular outgrowth which may have a pedicle or may be sessile. Not all polyps are adenomatous although most of them are—only a few consisting of fibrous, fatty or muscle tissue—possibly it is appropriate to use the term "adenomatosis" as a general term. In general, all polyps should be considered adenomatous until proven otherwise, and since aberrant or abnormal collections of glandular tissue carry a higher than average malignancy potential, such structures should be removed. This is particularly true of adenomatous structures in the colon, whether polypoid or sessile.

Single or several adenomas, polypoid or sessile, in a rectum or colon are clinical entities frequently encountered, differing from diffuse polyposis or adenomatosis which is not seen so often. Although such structures are most frequently found in adults, they are not uncommon in young children. About 5 per cent of all patients proctoscoped show polyps or adenomas. This condition of single or several adenomas does not present the serious problem of management as compared to the colon studded with innumerable tumors. Diffuse adenomatosis or polyposis was classified by Erdman and Morris[1] into two types: 1) acquired or adult, which is usually postinflammatory; 2) congenital or adolescent, with a heredofamilial factor, usually not congenital but developing in childhood. Occasionally it is found in infants, and McKenny[2] reported a patient 2 years of age. Dixon[3] reported two patients at the age of 18 months. This disease was first described by Virchow[4] in 1863, who found the condition in a 15 year old boy, but Cripps[5] in 1882 offered the familial tendency when he reported diffuse polyposis in a brother and sister.

The incidence of malignant transformation in any adenoma of the colon or rectum is high. Hullsiek[6] in 1928 collected a series of 127 cases of colon poly-

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posis and reported that 34.6 per cent were known to have cancer at the time the diagnosis of polyposis was made or the cancer occurred later during the period of observation. Scarborough[7] collected 301 cases in 1937 and reported a 50 per cent incidence of cancer. David[8], reviewing the subject from another angle, stated that 50 per cent of all carcinomas of the colon and rectum have flat raised areas of hyperplasia in close proximity to the malignant lesion and it is our impression that this figure is even higher. Strohl and Pontius[9] believe that 100 per cent of the patients with adenomatosis will eventually develop carcinoma.

The symptoms of single or several adenomas vary. Most frequently, the single adenoma, whether polypoid or sessile, presents no symptoms. However, some do bleed, others cause abdominal cramping or rectal fullness and urgency, and a few result in change of bowel habits, either constipation or increased frequency of stool. Occasionally one leads to intestinal obstruction, with or without intussusception. Symptoms are usually present in patients with diffuse adenomatosis but the degree of the symptoms varies considerably. Not infrequently, the symptoms are minimal, such as a tendency for stools to always be a little loose and numbering two to four daily, with no bleeding. Other patients present diarrhea, rectal bleeding or excessive amounts of mucus in the stools, urgency for stool, abdominal cramping, or intestinal obstruction partial or complete. Any patient with vague abdominal complaints and with any one or several of the aforementioned symptoms should be investigated for a possible colon polyp or polyposis.

The general physical examination of these patients usually reveals nothing of significance. The abdominal examination is usually negative unless a very large adenoma, benign or malignant, is present. The most important examinations are the proctosigmoidoscopic (not the simple insertion of a finger into the rectum) and air-barium double contrast enema studies of the colon. The proctosigmoidoscopic examination will identify small polyps and adenomas of the rectum and rectosigmoid region and the barium enema studies, including air-barium double contrast studies, will more frequently than not fail to identify lesions in this region. Single or several small adenomas of the sessile type, 2 or 3 mm. in diameter—the type most frequently seen—can only be identified by the proctosigmoidoscopic examination. Identifying these small adenomas which are the type so frequently found in the vicinity of malignant growths of the colon and destroying them, we believe is most important. Occasionally one is fooled in the endoscopic examination by what appears to be a small millet seed size adenoma only to be unable to locate it when the patient appears later for fulguration. We interpret these small false adenomas to be the result of local contraction of the muscular layers of the bowel wall throwing a fold of mucosa into a raised area which appears to be an adenoma. We do not believe one can identify these as such on a single endoscopic examination. A clean rectal wall is essential for this procedure. In our opinion, the proctosigmoidoscopic examination is the most important as it not only identifies the smaller lesions—single or multiple—but

when such lesions are found in the rectum, it immediately arouses the suspicion of other polyps or adenomas higher in the large bowel. An air-barium double contrast enema study must be made, and reporting the proctoscopic findings to the roentgenologist will assist him in identifying similar lesions at a higher level.

Obtaining satisfactory air-barium contrast enema films is an art. It requires additional effort and is more time-consuming. Our roentgenologist has produced excellent films by adding several tablespoonsful of tannic acid powder to a quart of barium solution, and we have rarely seen an impaction following such studies unless the emptying film reveals a poor functioning colon; then proper precautions are taken to prevent the impaction. Recently Marks[10] has advocated the incorporation of 2½ per cent methyl cellulose powder in the barium sulfate mixture.

Management

We agree with David[8] in his statement that all hyperplastic areas, whether polypoid or sessile in type, should be removed or the tumor completely destroyed as they are precancerous lesions and the transition from simple hyperplasia to adenoma or polyp to carcinoma is difficult to define or to recognize. It is our practice to take the time to explain clearly and in detail the significance of these rectal or colon lesions, whether single, multiple, large or small, and then in the future there is less difficulty in having these patients return for check-up proctoscopic examinations or colon x-rays.

A. Single or several polyps or adenomas in the rectum:—

1) Lesions within the last 6 inches and some of those to the 8 inch level are usually removed or fulgurated through the proctoscope and usually without any type of anesthesia. Occasionally a spastic, sensitive anal sphincter will require novocaine infiltration. We feel fulguration or removal of these tumors is a hospital procedure although frequently it is done on an out-patient basis. After one has experienced a hemorrhage from a pedicle or has labored with an inadequately prepared bowel, he becomes demanding in making this a hospital procedure. Occasionally a pedunculated tumor may prolapse through the anus, and the pedicle can be tied and transected. Insofar as possible, one should attempt to cut through the pedicle of the tumor with the high frequency electric snare or to fulgurate the pedicle until the tumor is released. Tumors measuring more than 5 mm. in diameter should not be destroyed without first obtaining some of the tissue for microscopic study. The small, sessile adenoma, no larger than 5 mm. in diameter, may be destroyed by fulguration or removal with the electric cutting loop. In all tumors, pedunculated or sessile, the base should be thoroughly fulgurated. A problem may arise if the small polypoid adenoma is reported back as malignant. We feel that with an adequate pedicle which has been thoroughly fulgurated, a "wait and see" attitude is warranted. The proctoscopic examina-

tion is repeated each month for 3 months, then at increasing intervals for 1 year. The patient is then checked every 6 months for 2 years. We have 3 cases now beyond the 3 year period where malignancy was present in a small pedunculated adenoma, and to date none has shown evidence of recurrence although treatment was limited to thorough fulguration of the pedicle. When the biopsy of a sessile type adenoma is reported back as malignant, an abdominoperineal resection or a rectosigmoidectomy with anastomosis is mandatory, regardless of the size of the lesion. With benign sessile adenomas having a base 1 cm. or more in diameter, local excision going wide and into the submucosal layer through a rectotomy incision after removal of the coccyx may be indicated. This is particularly true of the villiform growth in the rectum even though several biopsies have been negative for carcinoma. If malignancy is found in the base of the tumor, then radical rectosigmoidectomy with anastomosis or an abdominoperineal resection is indicated. Any induration or infiltration around the base of these tumors usually means malignancy even though microscopic study of the lesion shows benign papillary growth.

2) Single or several polyps or adenomas of the large bowel above the rectosigmoid area require abdominal exploration and colotomy. These patients must be prepared as for a colon resection. Through a longitudinal incision, the colon is opened. If the tumor has a long pedicle, it is ligated, transected and sent for frozen section study. If malignant without a doubt, a routine colon resection is done. If a sessile type of adenoma is found, a routine colon resection is done because in our experience such lesions in the colon above the rectosigmoid region are frequently malignant.

B. Polyposis or adenomatosis of the rectum and colon:—

This disease is relatively rare as compared to the patients seen with a single or just a few adenomas in the rectum or colon. Nevertheless it is not considered an unusual clinical diagnosis. The number of adenomas may reach many hundreds. The first bold attack upon this condition was made by Lilienthal[11] in 1901 as a two-stage procedure. At the first stage, an ileosigmoidostomy was done and at the second stage the right colon, transverse colon and left colon were removed down to the level in the sigmoid where the ileum had been anastomosed. The adenomas remaining in the rectum and rectosigmoid regions were not destroyed by fulguration. This patient was later reported as living 19 years following the operation. To have not developed a carcinoma after such a long period is most unusual. In 1923, Lockhart-Mummery[12] reported on a similar operation but he fulgurated the rectal adenomas. Coffey[13] in 1926 advocated ileostomy followed by a three-stage procedure, removing the entire colon and rectum. Hedin[14] in 1939, in an attempt to avoid total colectomy and a permanent colostomy or ileostomy, recommended multiple temporary colostomies through which the adenomas could be fulgurated by means of the proctoscope with later closure of the colostomies. Of course this can only be condemned, as experience with ful-

guration of rectal adenomas reveals the appearance of new adenomas and repeated observations and further fulgurations are needed. After closure of the temporary colostomies, this would be impossible. In the late 1930's some progress was being made by individual surgeons who were attempting in various ways to excise most of the colon, destroy the adenomas in the rectum, and restore intestinal continuity with a functioning sphincter mechanism. Mayo and Wakefield[15] advocated a 4 or 5 stage colectomy procedure after fulguration of the rectal adenomas, which included anastomosis of the ileum to the upper rectum or lower sigmoid. Other surgeons, including ourselves, managed such cases in a similar way, with a gradual tendency to lessen the number of stages. Recently, Boehme[21] has reported on the development of the technic of colectomy and sphincter preservation for adenomatosis. We[16] also completed some anastomoses of the ileum to the lower rectum or anus in 1940 as an experimental project because we had observed one of our own cases as well as one operated upon elsewhere where carcinoma developed in the rectal stump after fulguration of rectal adenomas. The operation of anastomosing the ileum to the anus had some complications which annoyed us as well as the patient and we reported these cases. Nevertheless we did not believe such a procedure should be abandoned, as improvement in technic could occur. In 1947, Ravitch[20] described a technic which we believe has some advantages. The two cases where malignancy developed after fulguration of rectal adenomas also annoyed us, but we finally concluded that this probably was unusual and that the patients had not been kept under sufficiently close observation for early fulguration of any developing adenomas. If this is true, then anastomosis of the ileum to the upper rectum after fulguration of the rectal adenomas is probably the operation of choice, and the operation of anastomosing the ileum to the anus should be reserved for those cases of adenomatosis where malignancy of the rectum is found near the 3 inch level.

Some surgeons, including Estes[17], Cattell[18], Strohl and Pontius[9], have definitely expressed themselves, stating that complete colectomy with a permanent ileostomy is the operation of choice because of the strong carcinogenic factor in patients with diffuse adenomatosis. We agree that additional adenomas tend to appear and that these adenomas have a strong carcinogenic tendency but believe that complete colectomy with a permanent ileostomy is probably a more radical procedure than is necessary. It is certainly debatable as to whether it is practical to give twenty or thirty patients the disadvantage of a permanent ileostomy because one of them might develop a carcinoma in the rectal stump. Again I wish to repeat that we believe the circumstances should be explained to the patient and that he should be permitted to have some choice in the matter.

We have a strong feeling against the complete colectomy with a permanent ileostomy, and we manage patients with adenomatosis in the following manner. Some lesions, both polypoid and sessile types, are removed by direct fulguration while others are removed by the wire loop electric current or the pedicle is fulgurated until the lesion is detached. Lesions larger than 5 mm. in diameter are

subjected to microscopic study. At times it is necessary to see the patient a number of times at the hospital on an out patient basis before all lesions are eradicated. We only go to the height of the first difficult angulation of the rectum in these fulgurations. After all adenomas have been completely destroyed, adequate preparations are made for subtotal colectomy in one or two stages, preferably in one stage. The ileum is anastomosed end-to-end to the mid or upper rectum and the remaining colon is removed.

For the first year, we have these patients return for proctoscopic examination every 3 months, and any new or remaining adenomas are fulgurated. During the second year, the patients are examined every 4 months and sometimes oftener. Under no circumstances should these patients go longer than 6 months without a check-up proctoscopic examination during the next 2 years, and thereafter they should be checked at least once a year. If a malignant tumor does develop in a patient, an abdominoperineal resection with a permanent ileostomy is usually recommended.

If a carcinoma of the rectum is found in addition to the adenomatosis when the patient is first examined, a more controversial problem is present. We do not believe that the individual carcinoma of the rectum in adenomatosis is any more malignant that the usual carcinoma of the rectum, and we favor operations for preservation of the sphincter mechanism insofar as possible[19]. If malignancy is found in an adenoma, either polypoid or sessile type, and it is at or above the 3 inch level, we destroy the adenomas of the lower rectum and accomplish a subtotal colectomy with anastomosis of the ileum to the lower rectum or anus. If recurrent carcinoma develops an abdominoperineal resection is done. If the lesion is below the 3 inch level, colectomy and abdominoperineal resection are indicated. We do not believe from our experience that the percentage of recurrent carcinomas in our rectal stumps is any higher than the percentage following abdominoperineal resection. Furthermore, if there is recurrence of the carcinoma, it is usually expressed by bowel symptoms and a proctoscopic examination may secure the diagnosis before it is impossible to make a second attack (abdominoperineal resection) on the lesion. In our experience, recurrent lesions following abdominoperineal resection are diagnosed too late to permit a second attack upon the lesion.

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Discussion

Dr. Morris L. Parker (Chicago, Ill.):—I wish to compliment Dr. Best on his paper, a really excellent presentation. The last time I talked with Dr. Best was in Cologne, Germany, at Von Heberer's Clinic, when we discussed surgery of the stomach.

The subject of polyps of the colon and the rectum is very interesting and timely, and at the same time offers a good deal of difference of opinion among surgeons, particularly, as to how radical or how conservative we should be. The chief reason for that is that there exists today much confusion concerning the histopathology of these lesions. Even the terminology applied to this group of new growths is confusing. One hears such terms as metaplastic, hyperplastic, pseudoadenomatous, papillomatous, atypical, precancerous and cancerous polyps.

An analysis of the literature reveals that we are confronted with two main concepts in the study of the histopathology of polyps. One, that of David, states that "invasion and infiltration is the principal sign of cancer; while the other signs of increased activity of epithelial growth are suggestive, they offer no conclusive proof". The other school (of Broders and Schiller) bases the diagnosis of cancer on altered cellular characteristics, namely: (1) hyperchromatic nuclei, (2) increase in size and irregularity of the nuclei, (3) atypical mitosis, and pseudostratification. Penetration of the basement membrane is not essential, they claim.

As long as the criteria used in diagnosing malignancy by the different authorities will vary, there will be difficulty and inaccuracy in comparing statistics and opinions.

We know that there is a definite relationship between adenomas and carcinomas of the colon and rectum, but there is no agreement as to the degree. Some authors think that only about 15 per cent of all polyps become malignant. Others think 50 per cent is more correct, while still others (Strohl and Pontius) believe that 100 per cent of all cases of adenomatosis will eventually develop carcinoma.

The most recent study of a series of 800 carcinomas of the colon and rectum (Bacon, et al) showed that in 11.25 per cent it could be definitely stated that the carcinoma developed in a benign adenomatous polyp, while in 3.75 per cent it could be presumed that the origin was similar.

The symptoms of polyps of the colon are well known. The most frequent one, however, by which its presence becomes evident is bleeding. Diagnosis is established by proctoscopic examination or double contrast enema, if the lesion is above the reach of the sigmoidoscope.

There are many patients with persistent bleeding of red blood where polypoid tumors of the large bowel are suspected but cannot be found despite repeated careful examinations. As a general rule, exploratory operations in such patients are not justified, as it is extremely difficult to find adenomas of the bowel by palpation of the colon unless they are fairly large or a definite part of the bowel is under suspicion. Transillumination of the bowel has been used to demonstrate the lesions at time of operation, with only fair success. Other lesions presenting much the same type of bleeding are Meckel's diverticulum, containing gastric mucosa, adenomas of the small bowel, malignancies of the small bowel, or localized granulomatous ulceration of the colon.

In the management of polyps of the colon and rectum it is now generally accepted that thorough removal by the simplest and safest method is indicated. About 70 per cent of all carcinomas and polyps of the large bowel are within easy reach of the sigmoidoscope.

In lesions below the peritoneal reflection, pedunculated lesions may be removed by ligation of the pedicle, well away from the adenoma, or by thorough fulguration through a proctoscope.

Areas of hyperplasia and sessile adenomas may also be fulgurated.

Ulceration and induration suggest malignancy, and several areas should be removed for microscopic study.

In lesions above the peritoneal reflection exploratory laparotomy and colotomy are performed, after thorough preoperative preparation as for bowel resection. If no signs of malignancy, such as ulceration, induration or dimpling of the bowel are present at the site of the tumor attachment, the tumor is removed by simple excision. If there is definite suspicion, actual presence of malignant change or reasonable doubt, resection is performed. If resection can be avoided, the risk of the operation is distinctly lowered. In the better clinics, the mortality and morbidity of the two are comparable, but this is not true generally.

We do not agree with the concept that routine resection of the colon should be done in all cases. Actually, carcinoma develops in about 14 to 15 per cent of polyps. We feel that it is not justifiable to do 7 colon resections to accomplish the proper operation for one possible cancer.

As to microscopic examination of a frozen section at the time of operation, most pathologists will not express a definite opinion except in well-developed and marked cases because it is impossible to be certain of the cytology by this method.

The operation for all carcinomas, no matter how small, should be radical, because of the impossibility of estimating with accuracy the tendency to metastasis in any given tumor. A major procedure, however, should not be performed as a prophylactic measure. The principle of fitting the operation to the patient instead of the patient to the operation, still applies.

Dr. Lynn A. Ferguson (Grand Rapids, Mich.):—I should like to endorse everything that Dr. Best has said and add a bit.

We are at present running a series of routine x-ray studies on colons which are asymptomatic. We have now considered well over fifteen hundred and the first 600 have already been reported upon. We find approximately 1.5 per cent operable pathology principally polypi, and, in one instance, a frank carcinoma of the transverse colon. Diverticula that do not produce symptoms are very common.

We do not trust any polyp. We believe that every polyp is a potential cancer, whether it be single or multiple. Whenever we have a colon open for polypectomy, we look each way with a proctoscope for fellow travelers. The hot snare and fulgurating equipment are always ready if needed. You would be surprised and intrigued by the number of small trivial polypi which do not show on the films.

Whenever we see a polyp in the sigmoidoscope, we note that this is a potential cancer patient, and is a potential candidate for a total or partial colectomy. We always try to preserve the rectal segment, free from polypi and

free from any stenosing pathology, always keeping in mind that sooner or later we may have to do an ileosigmoidostomy or a similar lower procedure as the case may demand.

I should like to go along with Dr. Best on the sphincter preserving idea, because it is perfectly possible to anastomose the bowel wherever you desire. It may be technically difficult to accomplish when low, but it can be done and, if carefully done, it is functional, which is not always the case with the pull-through operation. I do not hesitate, however, to use the pull-through operation if I think it is indicated, and try to be content with such functional result as is obtained.

Let's strive to cure our cancers in the polypoid stage. This means an alert examining finger, careful proctoscopy and the assistance of a painstaking roentgenologist. Our thanks to Dr. Best for his excellent coverage of the subject.

HEMORRHOIDS

Etiology, Pathology and Treatment

(Part III)

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Ligature and Excision Operations

No attempt will be made to discuss the large number of minor variations devised.

A practical modification of the Allingham ligature operation is that described by Hirschman in 1925. This operation, with minor modifications, may well serve as a basis for the majority of present and future ligature and excision technics in the United States.

It differs from the St. Mark's ligature operation in that the rectal mucosa overlying the hemorrhoids is excised and all the veins and the diseased tissue of the hemorrhoids are dissected out. The mucosal wound is partly closed by one or more sutures and becomes continuous with an external skin wound as indicated for adequate drainage. The detailed technic follows:

After adequate exposure with Pennington or other clamps, a double ligature transfixes the upper pole of the internal hemorrhoid at its junction with the normal rectal mucosa before any dissection is done (Fig. 21 A). The ligature is left long. A second suture may be passed for additional hemostasis. Allis or Kocher clamps are placed on the internal hemorrhoid and then on the skin in the radial axis of the internal hemorrohid. Additional clamps may be used as necessary for exposure (Fig. 21 B). With gentle traction, the clamps, the skin and rectal mucosa overlying the hemorrhoid are dissected up to within a quarter inch or so of the original transfixion suture (Fig. 21 C). The hemorrhoid is then cut away and tied, leaving a short stump (Fig. 21 D). Excessive removal of the rectal mucosa should be avoided in this dissection. The veins forming the main portion of the hemorrhoid and the so-called diseased tissue overlying the internal muscle are now carefully dissected out. The mucosal edges may be elevated to facilitate this dissection.

The long end of the ligature is now re-threaded on a small curved needle and the edges of the mucosa approximated as far distally as desired. Complete closure is not done. These sutures may, however, be reintroduced to control hemorrhage. Adequate skin drainage completes the operation (Fig. 22).

This is a simple and satisfactory ligature and excision technic. Care must be exercised to avoid strictures by overly wide excisions of the rectal mucosa

and particularly the anal canal skin — the anoderm. The external and internal sphincters likewise require due consideration.

This is a simple and satisfactory operation for the average case of internal hemorrhoids. The author, however, favors a technic which avoids incision or excision of the rectal mucosa above the intermuscular septum.

A modification of the Hirschman operation is a closed technic recently described by Elkins as the Fansler technic. The essential steps are as follows:

"The Fansler scope is inserted", and "removal of hemorrhoids is made in all four quadrants". The skin as well as the mucosa is completely closed

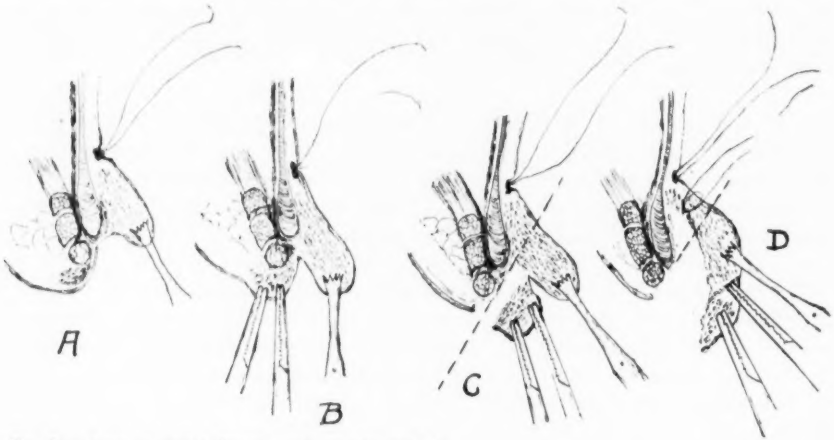

Fig. 21—Steps in simple ligature and excision technic.

A. Suture-ligature of upper pole of hemorrhoid at its junction with normal rectal mucosa. This suture may be double and is left long.

B. Traction forceps on body of hemorrhoid and the axially related external skin component.

C. Dissection of skin, external veins, anoderm and rectal mucosa overlying the internal hemorrhoid to within ¼ inch of the original suture-ligature. Dotted line is axis of incision.

D. Tieing-off the stump and excision of the hemorrhoid.

except in the "posterior quadrant" where the mucosa is sutured transversely to the distal margin of the external sphincter. Pectenotomy is done in one or more quadrants to "promote relaxation and healing".

These modifications appear to have given "results uniformly excellent" despite complete skin and mucosal closure and the removal of hemorrhoids in all four quadrants with "pectenotomy in all cases".

The author's objection to closed hemorrhoidal technics has already been recorded.

St. Mark's Ligature Operations

The St. Mark's Ligature Operation (Milligan and Morgan et al) is considered by the author as a highly satisfactory and anatomically sound operation with minimal postoperative complications and recurrences. The technic is as follows:

The anal canal is dilated as indicated. Allis or ordinary clamps are applied to the primary hemorrhoids which are retracted in their radial axes. Retraction of the 3 primary hemorrhoids forms a ridge or fold of rectal mucosa from one hemorrhoid to the other, the triangle of exposure (Fig. 23). This triangle assures simultaneous exposure of all 3 primary hemorrhoids with their pedicles as well as the secondary hemorrhoids without pedicles. No retractors are used.

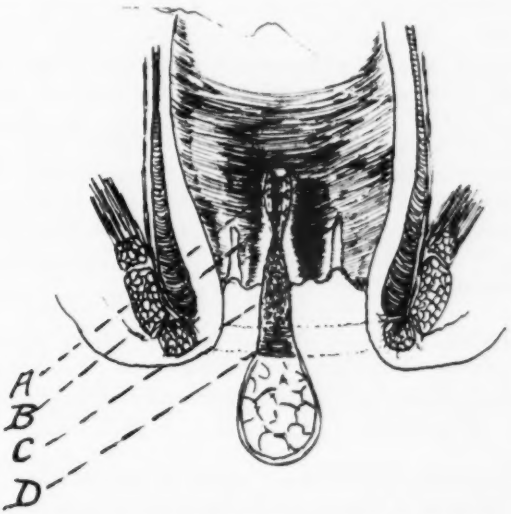

Fig. 22—Ligature and excision technic—longitudinal section.
A. Initial suture-ligature.
B. Partial closure of rectal mucosa.
C. The exposed bed of the hemorrhoid.
D. The subcutaneous external sphincter muscle.

Additional clamps are next applied to the skin in the same radial axes as the primary hemorrhoids for the skin dissection which is the next step. Additional clamps may also be applied below the Allis or pedicle clamps for better traction.

The anal canal skin dissection is made in the radial axis of the internal hemorrhoid. With the pedicle and skin clamp held in the operator's palm and the free index finger of the same hand in the anal canal a V shaped cut is made from the intermuscular or intersphincteric line to the outer edge of the external hemorrhoidal plexus. This dissection is carried through the corrugator cutis ani fibres

and should expose the subcutaneous external sphincter muscle from without inward. This is important. The subcutaneous external sphincter muscle must be identified. This dissection is facilitated by digital pressure against the sphincter muscle by the index finger in the anal canal (Fig. 24). The skin dissection should extend no higher than the inner border of the subcutaneous external sphincter in order to conserve those extensions of the conjoined longitudinal muscle below the intermuscular or intersphincteric septum.

Following the skin dissection the entire hemorrhoidal pathology now swings free on a pedicle which embraces the freed external veins, the outer terminal extensions of the conjoined longitudinal muscle and the internal hemorrhoid with any additional redundant rectal mucosa. The pedicle is now firmly retracted and transfixed.

It is our custom to transfix this pedicle in its center from above downward with a double #1 chromic suture or #2 plain, tieing each half of the pedicle and then the entire pedicle with the same suture, the knot on the lumen side. A minor but important point is to bring the transfixion needle out through the pedicle immediately above the upper or inner border of the subcutaneous external sphincter, which should be positively identified either by touch—index finger in the anal canal or direct visual exposure. It is to be emphasized that the transfixion suture contains no muscle except the few anchoring fibres of the conjoined longitudinal muscle—the corrugator cutis muscle.

When the pedicles are considered too large for simple transfixion the two-needle method may be advantageously used forming 3 or more small stumps on one side. Stricture and excessive scarring and secondary hemorrhage may follow if stumps are excessively large.

If the initial skin dissection does not afford adequate external drainage, which minimizes the incidence of edema and thrombosis, the postoperative pain producing factors, it should be enlarged accordingly.

Sufficient skin, however, should be conserved between the two right-sided hemorrhoidal stumps.

The skin dissection should not be continued above the upper margin of the subcutaneous external sphincter muscle. This is important. Dissection above this level permits retraction of the hemorrhoidal stump into the rectum proper and sacrifices the lining epithelium of the anal canal—the anoderm. Unnecessary high dissection or stripping may leave large raw exposed areas which predispose to delayed healing, excessive scarring and possible stenosis with its dyschesic sequelae. This technic was primarily devised to avoid these undesirable features and does so eminently.

The resulting stumps, of the usual three primary internal hemorrhoids, should finally lie no higher than the anal intermuscular septum (Fig. 26). Small secondary hemorrhoids in this technic are simply tied off directly, the ligature falling into a small incision in the mucosa at the lower edge of the hemorrhoid. A freeing incision into the perianal skin is not desirable nor necessary.

Iodoform gauze strips placed in the skin wounds and pressed in place with small one inch gauze pads together with a penrose drain or small soft rubber tube affords a simple effective dressing. Oxycel cotton may be substituted for the iodoform gauze.

It should be noted that this simple procedure removes the corresponding external veins, skin, infected interstitial tissue, the internal hemorrhoid and the prolapsed mucosa, and thus effectively and with the minimum of dissection, deals with all the hemorrhoidal pathology. It is quite unnecessary to dissect up the internal hemorrhoids into the rectum in order to remove them, they are simply drawn down to the lower level of the anal canal and tied off. *This of course pre-*

Fig. 23—The pedicles of the three primary hemorrhoids held and retracted by the pedicle forceps—"triangle of exposure". Note obstructure distention of external hemorrhoidal plexus. (*Reproduced by permission from The Lancet.*)

supposes that the hemorrhoid has a pedicle, and that actual surgical hemorrhoids with the typical distribution and not a more or less normal internal annulus hemorrhoidalis is to be subjected to this technic. When hemorrhoids require excision in the course of a fistula, fissure, submucus sinus, low tumors, etc., this technic is not so readily applicable and should not be used by those inexperienced in its use. Simple transfixion and excision is preferable in these cases. This operation has likewise a limited application in the hemorrhoidal patient with a complete ring of combined internal and external varicose tumors. Some modification of an amputative technic is indicated in these cases.

Ligature and Excision Operations With Clamps

Clamps of one variety or another have been used for many years in conjunction with ligature or cauterization. Hemorrhage was the bugbear of the hemorrhoid operation over the centuries and the ingenious, painful crushing devices to control it eventually developed into the modern hemorrhoidal clamps. The clamp

and cautery operation is still a somewhat popular technic especially in the hands of the general surgeon. Clamps, with but few exceptions, have no advantages over simple anatomical placement of ligatures. When the cautery was not used, the hemorrhoidal tissues engaged in a clamp were commonly transfixed through the center or upper end of the clamp and tied off above and below as the clamp was withdrawn. This procedure has no advantage over simple ligature without the clamp since the remaining stumps are as large, if not larger, than without it and their large size predisposes to postoperative hemorrhage. Simple ligature operations are gradually supplanting the clamp technics.

There are, however, a few definite indications in which the clamp with a running suture offers special advantage. These include the removal of large vascular redundant pedicles in the amputative types of hemorrhoidectomy, removal of large anal or rectal mucosal prolapse and particularly the removal of the so-called "perineal pile" and rectocele usually associated with prolapsing hemorrhoids in the female.

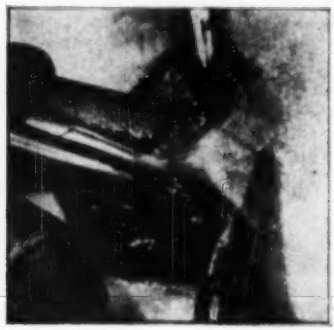

Fig. 24—Skin incision in the St. Mark's operation. It extends roughly from the external to the internal or upper border of the external hemorrhoidal plexus and exposes the structures as shown in Fig. 25. (*Milligan and Morgan et al. Lancet,* 1937).

In the "rectocele" the clamp provides a linear anterior rectal scar in contrast to the irregular scarring following a large ligatured stump. This sensitive area is predisposed to postoperative fissure and delayed healing.

Clamps for the above purposes should have serrated jaws and provide a firm even bite of sufficient length to include all the tissue to be removed (Fig. 27).

The clamp and running suture technic for the "perineal pile" usually associated with rectocele follows:

An adequate triangular-shaped skin incision in the anterior perineum is carried *only* as far as the outer margin of the subcutaneous external sphincter muscle which, in the female, at this point is very superficial and readily identified. The anoderm should not be stripped up into the anal canal or rectum as fissure may

follow. The rectal prolapse "perineal pile", and hemorrhoid, if present, are grasped in several Allis clamps and gently, but completely fanned out to the upper end of the prolapse. A #1 chromic suture—orientation suture—is placed in the rectal mucosa at the proximal end of the prolapse. Penetration of the rectovaginal septum is best guarded against by vaginal finger control (Fig. 28).

The clamp, up to the point of the orientation suture, now engages the prolapse. Care must be used in the application of the clamp to avoid including tissues under lateral tension which may be followed by tearing out of the running suture with a wide rectal wound. The clamp is primarily used to avoid this.

Following the excision of the redundant tissue above the clamp a running

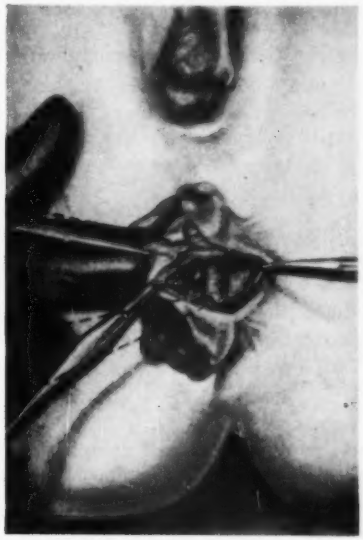

Fig. 25—Shows the proper depth for completely removing the external veins by exposing the subcutaneous external sphincter muscle and dividing the lower extensions of the conjoined longitudinal muscle—the corrugator cutis ani. (*Milligan and Morgan et al. Lancet*, 1937).

suture of #1 plain catgut is placed around the clamp with both ends left long (Fig. 29). Additional sutures may be placed below the running suture in cases with a vascular pedicle. These are tied after the clamp is removed and the running suture pulled taut and tied at its distal end. The upper and lower ends of the running suture should not be tied together. This technic if properly done will usually be followed by a thin linear incapacitating scar.

Clamp and Cautery Operation

Cauterization of hemorrhoids is also an ancient procedure. The actual "hot iron" as well as the stronger chemical agents were commonly used.

Nitric acid was one of the more popular cauterants. It was in fact this cauterizing agent which was originally used with the clamp by Cusak of Dublin around 1846. Some years later Mr. Henry Smith popularized the clamp method in England by using the actual cautery which was eventually replaced by the present electrocautery. The operation has since been referred to as the clamp and cautery operation for hemorrhoids. It was widely and effectively used with excellent results by many general surgeons and several outstanding proctologists among whom were Kelsey, Tuttle and Yeomans, who considered it the best operation for hemorrhoids despite the adverse criticism of Allingham, Mathews and many others.

The method is now largely abandoned at least by the proctologists in favor of the ligature and excision technics which present cleaner and more exact surgical dissection of the hemorrhoids on a strictly anatomical basis without cumbersome paraphenalia. In the presence of complications these are additional advantages over the clamp and cautery.

In the amputative technic the clamp and cautery would scarcely be applicable and even less so in the so-called modern "protoplastic or rectoplastic technics".

Amputative and Proctoplastic Operations

A complete and combined annular ring of both internal and external hemorrhoids usually with partial or complete mucosal prolapse is occasionally observed and it presents the difficult problem of adequate removal of this combined hemorrhoidal "cruller" without permanent anatomical and physiological damage (Fig. 30).

In these cases, there is no typical grouping of the internal hemorrhoids. The landmarks of the anal canal—dentate line—intermuscular septum and external subcutaneous sphincter are distorted or entirely obliterated. Partial or complete rectal or anal prolapse is commonly associated and highly significant to the contemplated surgery.

These are difficult cases and require special individually selected technics which have been described notably by Fansler, Buie, Eltinge, Whitehead and many others.

The external hemorrhoidal ring may be overly prominent by obstructive edema, thrombosis and vascular congestion and in such cases operative interference preferably should be postponed until resolution has taken place.

The Whitehead operation has been considered an indicated technic for these advanced cases. However, it has deservedly fallen into general disrepute on account of its unsatisfactory sequelae and it is now seldom employed. Complete amputa-

tion of the hemorrhoidal annulus is surgically unsound because suturing rectal mucosa to the anoderm or skin with equal tension throughout the anal circumference is difficult if not impossible, without some subsequent skin introversion or mucosal extroversion, usually the latter, the "Whitehead deformity".

Furthermore, the disabling and dyschesic complication following complete amputative technics are the loss of the normal anal sensorium together with a strictured or inelastic anal outlet. It may be further observed that complete amputation almost entirely destroys the sphincteric action of the conjoined longitudinal and puborectalis muscles. It is highly desirable therefore to preserve partial but complete continuity of the entire anorectal canal preferably in the sensitive commissures whenever this is possible.

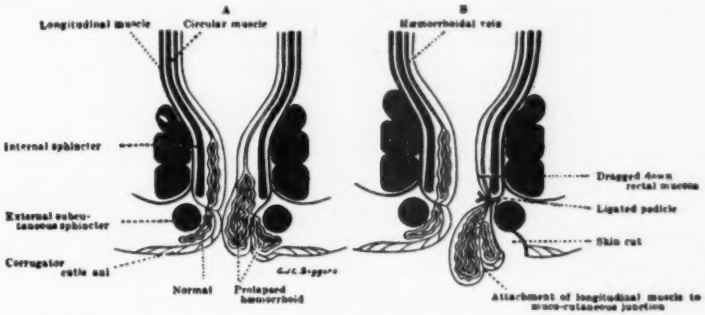

Fig. 26—Diagrammatic coronal section of anal canal. (A) Normal (on the left) and prolapsed hemorrhoids; (B) skin cut and ligation of pile pedicle. (*Milligan and Morgan*, Lancet 1937).

Amputative Technics

The preoperative preparation may advantageously include chemo- and antibiotic preparations which should be continued several days postoperatively. Thorough bowel preparation is highly desirable.

The jack-knife position with due regard to the tilted plane of the anal canal is preferred.

It is to be emphasized that no fixed operation is applicable to these advanced cases and regardless of the technic with or without a special clamp it is desirable that the complete continuity of the skin, anoderm and rectum be preserved in at least two or more quadrants if this be at all possible.

In view of the fact that the technic should be modified to suit the individual case, the author considers it useful to discuss general principles rather than details of technics which are available elsewhere.

The amputative technic devised and described by Buie is surgically sound and particularly applicable to cases with large secondary internal hemorrhoids. The clamp has special advantages in this operation in delineating the exact extent of hemorrhoidal tissue to be removed. The important point in the technic is the anchoring of the mucosal-skin suture line—the "new anorectal line" to the subcutaneous external sphincter muscle, to avoid skin introversion or mucosal extraversion. Sufficient mucosa without tension above the excised hemorrhoid as well as sufficient skin must be anticipated to avoid undue tension on the new suture line. The continuity of tissues in the commissures should remain intact.

Fansler has devised a technic in which he attempts to obviate the stricture and mucosal eversions of the old Whitehead operation by suturing skin flaps well up into the rectum. This technic is not simple and requires thorough knowledge of the anorectal anatomy. It requires careful dissection of all the hemorrhoidal tissue both internal and external, as well as no tension on the skin-rectal mucosal suture line. The exact level of the "new" anorectal line may be somewhat disappointing in this technic.

Hirschman has suggested an alternate procedure particularly designed to avoid stricture in these cases by not completely separating skin from mucous membrane but forming three eliptic flaps between which the continuity of the skin anal canal and rectum are preserved. The pathologic tissue below these flaps is removed but their continuity remains intact. Excessive skin tags which are apt to follow but are of no significance are subsequently removed.

In some cases the anal prolapse, rather than the internal hemorrhoids, is prominent. The author has used the following technic to advantage. With the specific idea of preserving the continuity of skin, anoderm and rectum in the commissures two sutures are introduced through both layers of the prolapse from below upward about one centimeter from the anterior and posterior midlines, and the knot tied on upper flaps. A similar suture is placed in the same manner just lateral to those already introduced. Incisions are then made in the mucosal hemorrhoidal fold between the through and through sutures. Hemorrhage may be controlled by additional fine catgut sutures as necessary. This forms two large lateral flaps which may be removed by successive ligature, over a clamp or by the two needle method which makes three stumps. The skin should not be included in this technic.

The prolapsed tissue in the commissures must be conserved. It retracts to some extent but may become thrombosed and edematous, and leaves a residual skin tag. This is removed after complete healing has transpired.

If desired, sutures may be placed laterally and four flaps made for subsequent removal (Fig. 31).

It is to be emphasized that all of these technics mutilate the anorectal canal from the anatomical as well as the functional or physiological standpoints. The simplest technic applicable to the well-studied and individualized case should be used. Simple secondary removal of skin tags or even additional hemorrhoids is much to be preferred to a "frozen" anal outlet following over-enthusiastic circumcision of the anal canal.

Because of the larger defects, poor drainage and sutures often under tension, these cases require good postoperative care with antiseptic irrigations, continuous moist dressings, frequent sitz baths and the necessary sedation to allay sphincterismus and pain. A small soft rectal tube, iodoform or oxycel strips in the wounds comprises the usual immediate postoperative dressing.

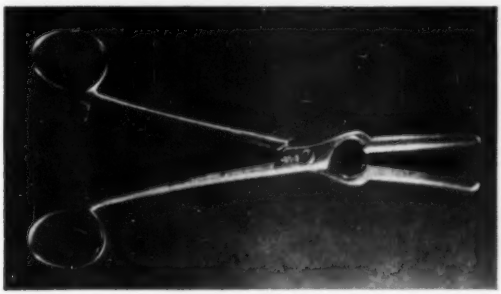

Fig. 27—Hemorrhoidal clamp for amputative procedures.

Electrical Methods

Electrical methods less commonly used in treatment of internal hemorrhoids, include medical and surgical diathermy, electrocoagulation, dessication, galvanism and ionization.

Medical diathermy is an ambulatory procedure and may be of some palliative value in the treatment of conditions associated with the hemorrhoids rather than the hemorrhoids themselves. It may prove useful in aiding the decongestive process of hemorrhoids following pregnancy, also in the relief of those sometimes intractable cases of anal neuralgia, sphincteralgia or spasm and coccygodynia sometimes associated with hemorrhoids. It may also be combined with other modalities and afford some benefit in constipation and portal congestion.

Surgical diathermy, coagulation, dessication, etc., are only mentioned for completeness. Experience shows that they aim to accomplish, by complicated and uncertain methods, what can be much more readily and easily done by the injection method or by simple ligature and clean surgery. Electrical methods are highly vaunted as being bloodless, sealing up the vessels and lymphatics, which is erron-

eously thought to be a decided advantage. Actually, as already noted, the majority of hemorrhoids have chronic submucosal infection, with possibly infected crypts, anal glands and skin tabs, etc. Removal of these and proper subsequent drainage with incision of the sphincter is usually essential to adequate treatment and satisfactory end results. Moreover the blood loss in a properly performed surgical operation for hemorrhoids is quite negligible.

In the surgical treatment of hemorrhoids, they offer no advantages over existing methods and should be abandoned, at least by the legitimate proctologist.

Sphincterotomy In Hemorrhoidectomy

Posterior sphincterotomy which divides the entire subcutaneous external sphincter as a minimum procedure is a variant which requires individualization and experience.

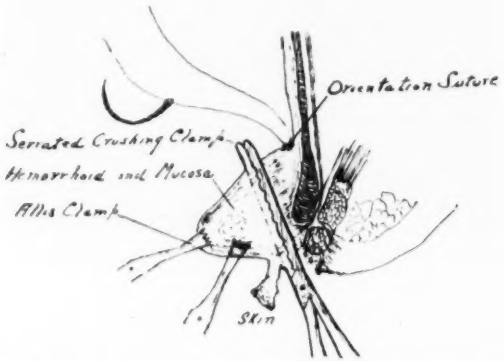

Fig. 28—Application of clamp to the retracted hemorrhoid and prolapsed mucosa following skin-freeing incision. Note that the clamp is placed far enough from the muscles to avoid their subsequent inclusion in the running suture to be placed below the clamp.

Its definite indications include, advanced fibrosis "anal pectenosis" and the "pecten band", particularly in the posterior anal phase; chronic anal fissure, and excessive preoperative sphincter spasm. In advanced hemorrhoidal disease, in which postoperative stricture is considered at all possible, sphincterotomy is definitely indicated and may prevent an undue amount of painful postoperative dilatation. The undesirable sequelae of a strictured and dyschesic anal outlet have been repeatedly emphasized.

Sphincterotomy may also be indicated in the heavy muscular individual who notoriously has a painful and protracted convalescence.

It is also indicated in cases where a large prolapsing hemorrhoid has been removed in the posterior midline.

Sphincterotomy includes adequate posterior triangular or racquet shaped skin drainage. The posterior level of this wound should approximate the level of the deepest portion of the sphincterotomy wound.

The preoperative injection of Anucaine in our hands has further promoted muscular relaxation and smoothed the postoperative course.

Sphincterotomy may also be done laterally through the skin excisions below the hemorrhoidal stumps as advocated by Gabriel. In our experience this has not proved as satisfactory as the posterior site in as much as the pathological indications for sphincterotomy are usually posterior. Moreover the posterior sphincterotomy more completely "defunctionalizes" the anal musculature. Lateral sphincterotomy also requires adequate skin drainage to avoid pocketing and subcutaneous fistulization.

Postoperative Care

The usual postoperative routine is as follows: Where the anesthesia has been spinal, the prone position is preferably maintained for six or more hours. For sedation two tablets of Emperin Compound with Codeine, grains ½ are given every four hours during waking hours. Demoral, morphine, dilaudid with atropine are administered hypodermically as necessary for pain. Hot compresses are grateful and hot sitz baths are used as soon as practical. For sleep, any of the barbiturates are used in appropriate dosage and repeated as necessary.

For retention, prostigmine 1-2000 by needle is given for three doses at hourly intervals. If unsuccessful, catheterization follows within ten hours postoperatively. In the occasional cases with urinary difficulty, doral or urochlorines are administered in tablet form, but not by needle.

On second or third postoperative day, catharsis using Phosphosoda sodium sulfate—Glaubers Salts—in three or four dram doses is given early in the morning, followed directly by the rectal instillation of three ounces of mineral oil to which ½ oz. of Topogesine has been well mixed. This affords some alleviation to the first defecatory effort which is feared by the average patient. Sitz baths are given immediately following the first evacuation and continued as desired. Subsequent catharsis by Zymenol, Metamucil or ordinary mineral oil is continued until normal bowel movements are established.

The diet is regular throughout, the only restrictions being foods to which the patient is definitely allergic or idiosyncratic. Postoperative dilatation is done only as indicated. The introduction of the finger is used to smooth out the anorectal wounds as much as to dilate the anal canal.

Postoperative Complications and Their Treatment

With proper selection of cases, careful preoperative preparation, selective anesthesia, and the modern ligature technics, serious postoperative complications are now comparatively rare. Minor complications however, are fairly common. Complications are immediate or remote.

Immediate postoperative complications are severe pain, hemorrhage, urinary retention, infectious or embolic processes and rarely ileus. The remote complications which may provoke considerable functional disturbances include fissure, "skin tags", stenosis of varying degree and a neurosis. These may be obstinate conditions.

Pain

Since the passing of the "whistle" and the intestinal splintage with opium compounds, the hemorrhoid operation has lost some of its reputation as the most

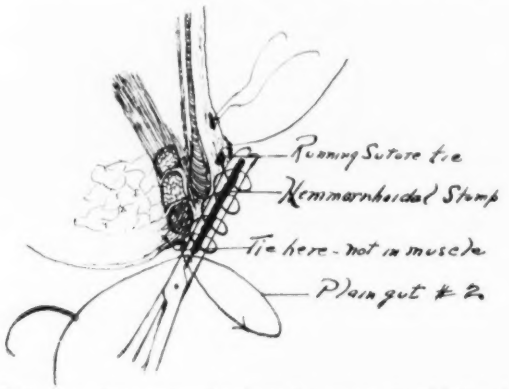

Fig. 29—Redundant tissue removed and running suture placed below the clamp.

painful of surgical procedures. Much has been written concerning the relation of pain to the various types of operations. The reports have been at great variance, tinged with personal enthusiasm for one method, and in view of the wide variation in individual fortitude, emotional state and the abuse of narcotics, their epicritic value in relation to pain is quite equivocal.

However, regardless of the operation or its execution, there are several factors, which in the author's experience are more apt to provoke a painful postoperative course. These include: large hemorrhoidal stumps which tie in the anoderm or skin in the strangulating ligature, edema, thrombosis and phlebitis due to inadequate skin drainage and/or severe spasm of the anal sphincters; traumatic fissures in the commissures, particularly the so-called high lying fissure in the posterior aspect of the anal canal; inclusion of the muscles in the ligatures or clamps and finally divulsion of the sphincter.

Postoperative Hemorrhage

Immediate postoperative hemorrhage is less common than secondary hemorrhage which usually occurs between the fifth and ninth postoperative day and probably results from the premature separation of the ligature on a sloughing stump. It may be of arterial or venous source. Overstraining during an obstructive defecation is usually the immediate or precipitating cause. Hemorrhage is sometimes concealed and evacuations are inhibited. Considerable blood loss may sometimes occur undetected and the systemic signs of pallor, faintness, rapid pulse and low pressure supervene. The rectum usually becomes intolerant and large clots with free blood are evacuated. Careful digital examination of the rectum usually confirms the hemorrhage.

Morphine, or demoral with synkovite and thromboplastin should be given at once and the patient's blood typed.

In mild cases, simple pressure on the hemorrhoidal area by the introduction of hemostatic gauze or cotton through a small anoscope may suffice. However, the patient must be carefully observed and if bleeding still persists, time should not be wasted. The trauma incident to the various methods of packing the rectum usually described may aggravate the bleeding. Rolens however has described a simple and nontraumatic procedure which may prove effective.

In the severe cases, the surest method is to transfix the bleeding point or points which are usually observed around the stumps of the larger primary hemorrhoids. The anesthesia is preferably intravenous pentathol or spinal. A small rectal tube, surrounded with hemostatic gauze, should be placed in the rectum. This should be kept patent by the occasional injection of normal saline. Blood transfusion may be indicated by the blood count. Cases of poor "clotters" and very rarely hemophilia calcipriva, or true hemophiliacs are encountered.

Urinary Retention

This occurs somewhat more frequently in males and after spinal anesthesia. Its incidence varies considerably from 5 to 40 per cent. It is commoner in cases with severe anal sphincter spasm and measures directed to allay spasm and stimulate the parasympathetic nerves are indicated. Packing and obstructive dressings and tubes should be removed from the anal canal, moist, hot compresses applied and antispasmodic drugs administered hypodermically. Catheterization may be necessary and if repeated, chemotherapy should be started. The preoperative injection of Anucaine will reduce the incidence of catheterizations by about 50 per cent as noted by Green and repeatedly confirmed by the author.

Infections and Embolic Processes

A thrombophlebitis is extremely rare but formidable. If in the superior hemorrhoidal radicals it may remain undiagnosed until a fulminating septic reaction,

with sudden pyrexia, chills, leucocytosis, etc., arouses suspicion. A digital examination of the rectum may reveal a diffuse, tender, boggy swelling or a localized abscess. Blood cultures may be positive and are indicated without delay.

Thrombophlebitic processes in the external veins usually complicate a cellulitis. Local pain, induration, redness and a brawny edema, which spread fairly rapidly indicate a virulent process, the streptococcus anaerobic and microaerophilic organisms should be suspected. Tetanus has been reported.

With antibiotic therapy, embolic processes are now fortunately very rare. Several different pathways appear to be traversed from the hemorrhoidal areas. These include the inferior sacral or middle hemorrhoidal veins into the inferior vena cava to the pulmonary capillaries. Emboli arising in the superior hemorrhoidal radicals usually reach the liver and produce multiple pyemic abscesses.

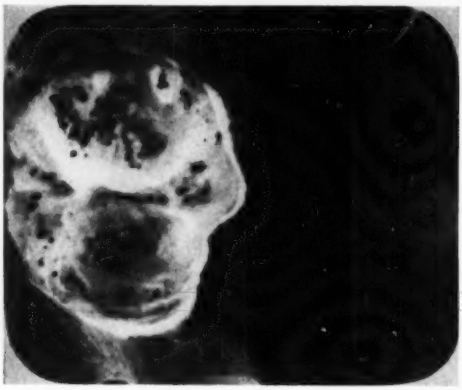

Fig. 30—Large prolapsing internal hemorrhoids with a ring of external hemorrhoids and hyperplastic perianal skin—"the hemorrhoidal cruller" in which an amputative type of hemorrhoidectomy is indicated.

These processes are more apt to occur in debilitated individuals with lowered resistance and undiagnosed systemic disease, diabetes, hepatitis, blood dyscrasias, agranulocytosis, etc.

Treatment

Treatment should be prompt with active supportive measures, blood transfusions, and antibiotics both intramuscularly and intravenously. It is imperative that the causative bacteria be determined forthwith either by blood culture or more directly by aspiration of the tissues. Anaerobic culture should not be overlooked. The further use of the antibiotics should be laboratory controlled. Frank abscesses require drainage without delay.

Adynamic Ileus

This is a rare immediate complication, described by Abel and Frankfeldt. It appears to be an an inhibitive process arising reflexly from the anal innervation. It may usually be readily differentiated from an obstructive ileus by auscultatory examination of the abdomen together with flat radiograms. Treatment is by decompression through a Miller-Abbott tube.

Fissure

Of the more remote complications, one of the commonest is the chronic anal fissure, which is usually associated with some degree of anal fibrosis, and stenosis. It may be a highly painful lesion and provoke considerable discomfort aside from defecation. The so-called high lying fissure with more or less levator spasm, coccygodynia and back pains is commonly misdiagnosed. It may be extremely intractable. It results primarily in a failure to establish adequate drainage particularly in the commissures. The advantages of a sphincterotomy as a prophylactic measure in avoiding fissure and anal stenosis has been previously emphasized. Fissure also results from large scars in the commissures which immobilize the anoderm and predispose it to repeated rupture.

Persistent and prolonged anal spasm, provoked by minor but irritating lesions in the anal canal, overlooked during the hemorrhoidectomy, is also a cause for fissure. These include an actual "cryptitis", pectenosis, pecten band, sentinel polyp, local proctitis and small submucus fistulae. There are too many patients who unhappily antedate their present rectal complaints to previous proctologic surgery.

Finally, fissure arises from the continuous sphincter spasm commonly found in patients with an anxiety syndrome or the so-called spasmophilic patient. These fissures are particularly resistant to ordinary palliative measures.

Sphincter spasm and a tendency to stenosis appear to be the main deterrents to sound healing. Treatment consists in maintaining free drainage, periodic dilatation, and the avoidance of defecatory trauma by laxation. Stimulating applications may sometimes be useful. Occasionally, complete dilatation or sphincterotomy under anesthesia is necessary for permanent relief.

Skin Tags or Tabs

These are "hemorrhoids" complicating hemorrhoidal operations. Regardless of the technic these troublesome excresences occur in an appreciable number of cases.

They result from a circulatory embarrassment in the anoderm or true skin, with an associated lymph edema and cellular sluding which are the more im-

portant etiological factors. Infection, thrombosis and tissue anoxemia are of additional significance. The essential histology as already noted, is an hypertrophy of the connective tissue elements of the skin, a fibrosis which recedes with gradual re-establishment of the circulation and lymph drainage. They should not be too hastily removed. Considerable reduction in their original size usually occurs, following re-establishment of the circulation.

It may be useful to emphasize that preservation of the elasticity of the anal musculature and canal is vastly more important than efforts to avoid skin tagging by the excessive removal of anoderm and skin. The patients should be so advised. After complete resolution and healing in the adjacent skin areas the skin tags may be removed by simple oudinization or excision under local anesthesia if desired.

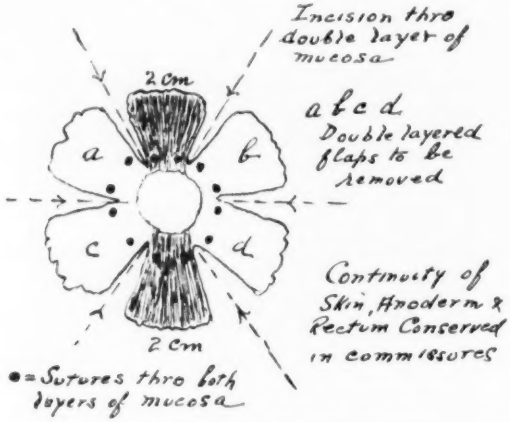

Fig. 31—Modification of amputative technic.

Anal Fibrosis—Stenosis

Much commoner than usually reported, this complication follows faulty technic or/and poor postoperative care. The degree of actual stenosis or fibrosis varies considerably.

It may involve the entire anal canal as well as the skin at the anal verge. The commonest site is the level of intermuscular septum. The most functionally disabling site is the level of the anorectal muscle ring, the puborectalis sling.

It may be scarcely noticed by the patient and with chronic laxation may be well tolerated unless other urgent symptoms supervene. On the other hand it may be highly obstructive, with a defecophobia and neurotic train of symptoms. The cases may be conveniently divided into those presumably amenable to systematic dilatation and those requiring further surgery.

It may be useful to point out however, that some cases with only a partial stenosis have associated symptoms of defecatory obstruction particularly with formed stools, excessive evacuatory bleeding, dyschesia, straining, sense of incomplete evacuation, other dyasthesias and sometimes an anxiety neurosis or cancerphobia. These symptoms may be caused by a residual anal fibrosis, or excessive scarring which produces a chronic sphincter spasm entirely aside from the stenosis. The treatment of these patients may be difficult and they require careful and cautious management.

Unless contraindicated, an injection of an oil soluble anesthetic (Anucaine) into the postanal tissues followed by systematic dilatation for several weeks is done for an accurate evaluation of the complaints as well as an index for the probable success of future surgery. If the response is unsatisfactory a posterior sphincterotomy should be considered.

In the advanced cases surgery is indicated and should be done without further ado. There is scarcely a simple operative procedure which affords a greater degree of permanent relief and satisfaction if properly done.

Since the anal landmarks are usually obliterated, the surgery must be done entirely on the recognition of the levator ani muscles, the puborectalis sling or anorectal muscle ring. Satisfactory results usually require complete division of the fibrosis and musculature up to the *lower posterior margin* of the anorectal ring. A detailed knowledge of the anatomy is essential. This incision is best carried out under digital control and followed by adequate posterior skin drainage. The sacral end of this drainage wound should be on the same level as the puborectalis sling-anorectal ring.

Convalescence may be shortened by freeing up the rectal mucosa posteriorly and suturing it to the mediolateral margins of the incision. No tension should be used. This provides a mucosal surface and improves the elasticity of the "new" anal canal. We consider it inadvisable to suture any skin flaps into this incision. This invites fistulization which may require additional disconcerting surgery.

The common causes of recurrences are: failure to divide the anal fibrosis completely up to the lower margin of the puborectalis sling and to provide adequate posterior skin drainage. An unrelieved anal stenosis may develop intractable neurosis, or hypochondriasis.

Neurological Complications

These are not common following hemorrhoidal surgery but they are usually intractable.

Occasionally a local irritative or painful lesion, adherent anoderm, scarring, crypt or sinus may explain the nervous symptoms. However, these patients commonly have an anxiety complex and their complaints are not justified by a meticulous and often repeated examination.

It is usually inadvisable to subject these patients to any further surgery in the absence of specific indications. We have observed several cases in which the surgical experimentation merely fixed the neurosis. Psychiatric consulation may be helpful.

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EDITORIAL

Dr. Max Einhorn,—on the Ninetieth Anniversary of His Birth

HYMAN I. GOLDSTEIN, M.D.

Camden, N. J.

Doctor Max Einhorn of New York City, and internationally known gastroenterologist, was born January 10, 1862 (some state the year is 1860). In March 1884 his first medical publication appeared: The Inaugural Dissertation (March 21, 1884, Berlin) on "Lymphocytes—" In 1887, Doctor Einhorn began to interest himself in the field of *gastroenterology* in New York City and environs. He had worked with Carl Anton Ewald in Berlin in 1888, for four months and upon his

Max Einhorn, M.D.

return to New York, assisted Doctor J. Rudisch (1847-1926). Doctor Einhorn also worked with Abraham Jacobi (1830-1919), the young Louis Conrad (1868-1895), and later, treated many of Jacobi's and Rudisch's patients. Doctor Einhorn knew and studied under Paul Ehrlich (1854-1915), during his visit at Ehrlich's laboratory. He also was befriended and encouraged by Gustav Adolf Langmann (1843-1916), Carl Lellmann and, the noted Salkowski and H. L. F. Helmholtz! Doctor Einhorn attended the Friedrich-Wilhelm Gymnasium, and in 1879

he entered the government gymnasium in Riga. He was enrolled as a medical student in St. Wladimir University in Kiev. He continued his medical studies, in 1881, in Friedrich-Wilhelm University in Berlin. He began general practice in Harlem, New York City in June 1885, and, in October 1885 became house physician (internal medicine division) in the German Hospital—now the Lenox Hill Hospital, and physician in the German Dispensary. On March 30, 1892, he was married to Flora Strauss of New York. He was for many years connected with the New York Postgraduate Medical School as instructor (1889), associate professor, professor, and (1922) Professor Emeritus and Consulting Physician.

Doctor Einhorn had the unusual privilege and opportunity to do some experimental work in the Frerichs Clinic, under Ehrlich in 1883, working on diabetes mellitus (in frogs). At the Friedrich-Wilhelm University (Berlin) (1881-1884), while carrying on his medical studies he met Rudolf Virchow (1821-1902), H. L. F. Helmholtz (1821-1894), Salkowski (1844-1921), Herman Senator (1834-1911), von Bergmann (1836-1907), von Leyden (1932-1910), and Paul Ehrlich (1854-1915)—what an array of famous men in clinical medicine and in research!

He received his Doctor's Diploma—magna cum laude—in March 1884, and in April 1885 he was licensed to practice medicine in Germany. For these examinations he left New York City for a brief visit to Berlin, in April 1885, returning to New York in June 1885. During his brief first visit to New York City in 1884, arriving on the "S.S. Katie" (Stettin-Lloyd) on which he served as ship's physician, he met Doctor Samuel James Meltzer (1851-1920). The many worthwhile contributions to gastroenterology, and to medicine in general, and the nearly 250 scientific publications contributed by Doctor Einhorn to the rapidly expanding and very extensive medical literature now fast accumulating in the field of gastroenterology, are well-known to the profession and need not be listed here!

Doctor Einhorn, the humanitarian, the clinician, the gentleman, and my good friend these past forty years, I salute you, and I wish you well during your advancing years, on this, your ninetieth birthday anniversary!

You are the living exemplar in America of the Old School—of *men*—men like Ismar Boas, Carl A. Ewald, Lenhartz, John C. Heimmeter, Lambert, Raoul Bensuade (France), Knud Faber, Francois Moutier and René Gutmann, Janeway, Walter B. Cannon, Joseph Sailer, Thomas R. Brown, Franklin W. White, Brinton, Samuel J. Meltzer, D. D. Stewart, C. C. Stockton, H. W. Bettmann, W. G. Morgan, I. W. Held, C. D. Aaron, Jacob Kaufmann of New York, Julius Friedenwald, Anthony Bassler and Horace M. Soper, (both still active, and youthful as ever), and our living and active investigator Anton J. Carlson, and *the pioneer men in gastroenterologic roentgenography*—Henry Hulst, Hermann Rieder, Francis H. Williams, J. C. Hemmeter, G. G. Burdick, Biggert, Walter B.

Cannon, Rudolph Brauer; Guido Holzknecht and Martin Haudek of Vienna; the late Franz M. Groedel, A. E. Barclay, Carl Beck, Donath, Arial W. George and R. D. Leonard, R. D. Carman, George E. Pfahler and H. K. Pancoast, E. A. Graham and W. H. Cole; F. A. Baetjer, and Leon LeWald, (alive and still active). Doctor Einhorn received many honors during the past five or six decades. Doctor Einhorn was a founder (1897) of the American Gastroenterological Association and is an Honorary member of the National Gastroenterological Association and of the International College of Surgeons, and also, of the German Society for Digestive Diseases, the Gastroenterological Society of Mexico, and the Gastroenterological Society of Japan, and corresponding member of the Medical Society of Munich and of Paris. He received the second Julius Friedenwald award in June 1942. In America, Doctor Einhorn, ably and fully represented the Ewald-Boas School of Gastroenterology–and, as the German poet J. M. Friederich Ruckert wrote–: *Schön ist es überall, ein Stellvertréter zu gelten für die Welt, und nicht für Sich allein*"–of great prophets and teachers!

"Glorious it is everywhere, to take another's place,

To be worthy of the world, and represent the race."

To you my friend Doctor Einhorn on this, your ninetieth birthday anniversary, may I say with Dixie Wilson:

"Count your gardens by the flowers,–
Never by the leaves that fall.
Count your day golden hours–
Don't remember clouds at all!
Count your nights by stars–not shadows,
Count your life with smiles–not tears.
And with joy on this, your birthday,
Count your age by friends,–not years."

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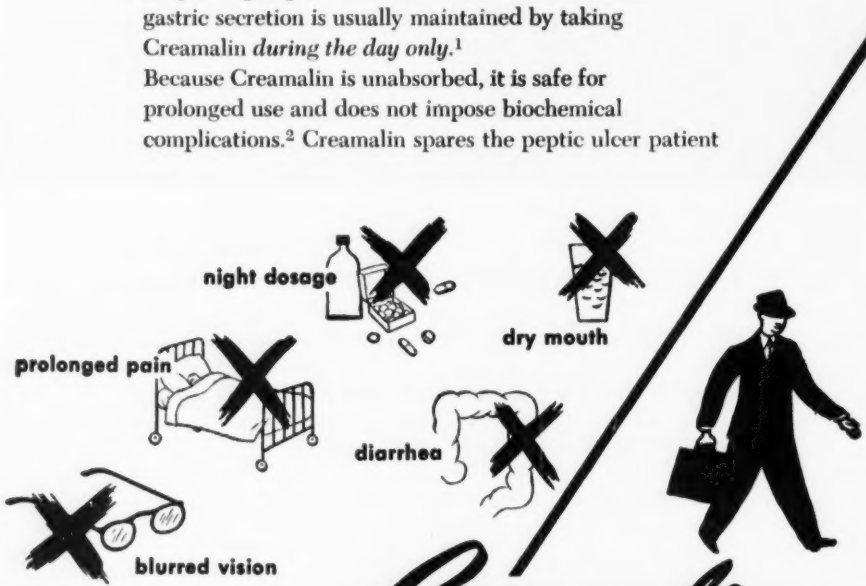

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*Kramer, P. and Ingelfinger, F. J., Med. Clin. North Amer., 32:1227, 1948.
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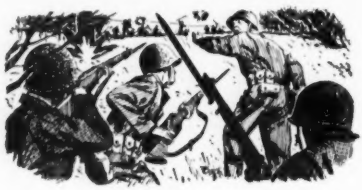

assault up the fire-swept hill. In the traditional Infantry spirit, Captain Millett charged into the enemy positions, bayoneting two of his foes, then shouting encouragement to his troops, continued throwing grenades, and clubbing and bayoneting the enemy. Inspired by his example, the attacking unit routed the enemy, who fled in wild disorder.

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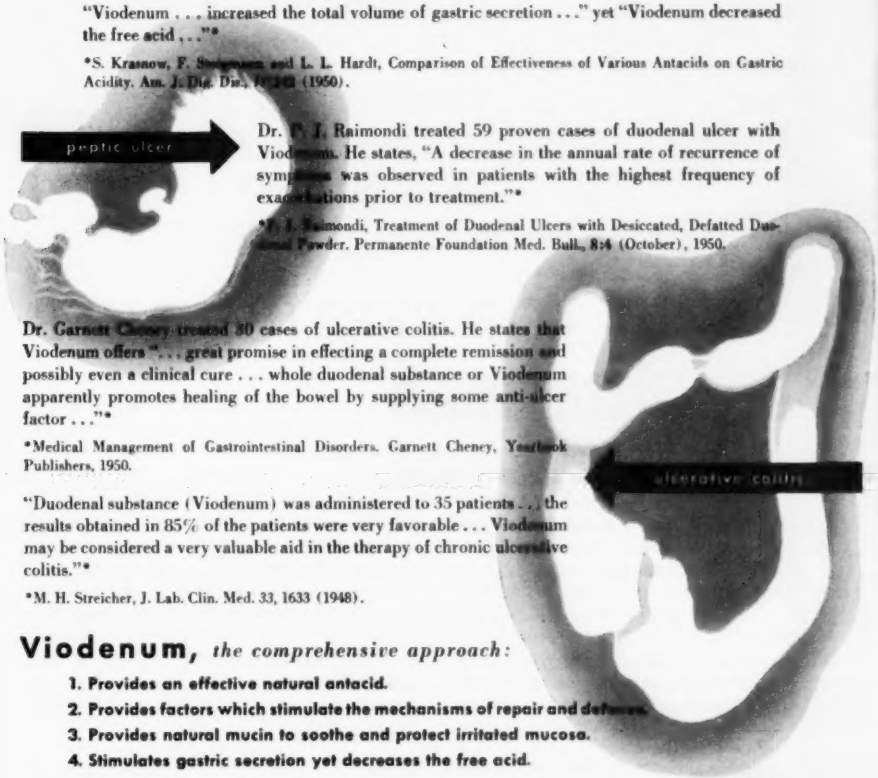

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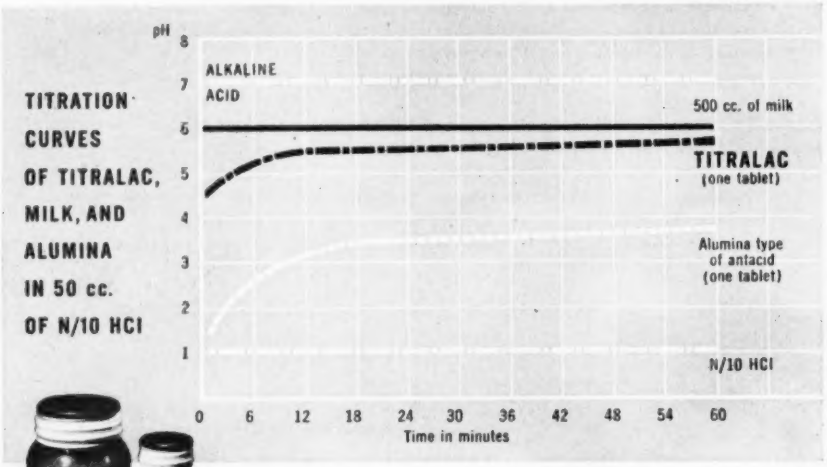

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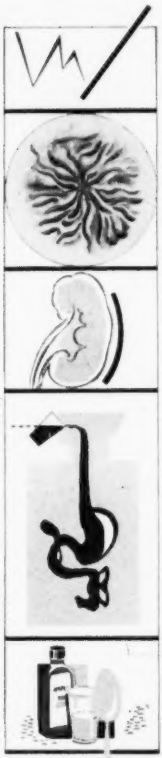

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